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(54) Title: CHIMERIC PROTEINS COMPRISING BORRELIA POLYPEPTIDES: USES THEREFOR

(57) Abstract

Novel chimeric nucleic acids, encoding chimeric Borrelia proteins consisting of at least two antigenic polypeptides from corresponding and/or non-corresponding proteins from the same and/or different species of Borrelia, are disclosed. Chimeric proteins encoded by the nucleic acid sequences are also disclosed. The chimeric proteins are useful as vaccine immunogens against Lyme borreliosis, as well as for immunodiagnostic reagents.

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CHIMERIC PROTEINS COMPRISING BORRELIA POLYPEPTIDES: <u>USES THEREFOR</u>

Background of the Invention

- Lyme borreliosis is the most common tick-borne infectious disease in North America, Europe, and northern Asia. The causative bacterial agent of this disease, Borrelia burgdorferi, was first isolated and cultivated in 1982 (Burgdorferi, W.A. et al., Science 216: 1317-1319 (1982); Steere, A.R. et al., N. Engl. J.
- Med. 308: 733-740 (1983)). With that discovery, a wide array of clinical syndromes, described in both the European and American literature since the early 20th century, could be attributed to infection by B. burgdorferi (Afzelius, A., Acta Derm. Venereol. 2: 120-
- 15 125 (1921); Bannwarth, A., Arch. Psychiatr.
 Nervenkrankh. 117: 161-185 (1944); Garin, C. and A.
 Bujadouz, J. Med. Lyon 71: 765-767 (1922); Herxheimer,
 K. and K. Hartmann, Arch. Dermatol. Syphilol. 61: 57-76,
 255-300 (1902)).
- The immune response to B. burgdorferi is characterized by an early, prominent, and persistent humoral response to the end of lagellar protein, p41 (fla), and to a protein constituent of the protoplasmic cylinder, p93 (Szczepanski, A., and J.L. Benach,
- Microbiol. Rev. 55:21 (1991)). The p41 flagellin antigen is an immunodominant protein; however, it shares significant homology with flagellins of other microorganisms and therefore is highly cross reactive. The p93 antigen is the largest immunodominant antigen of
- 30 B. burgdorferi. Both the p41 and p93 proteins are physically cryptic antigens, sheathed from the immune system by an outer membrane whose major protein constituents are the outer surface proteins A and B

(OspA and OspB). OspA is a basic lipoprotein of approximately 31 kd, which is encoded on a large linear plasmid along with OspB, a basic lipoprotein of approximately 34 kd (Szczepanski, A., and J.L. Benach, Microbiol. Rev. 55:21 (1991)). Analysis of isolates of B. burgdorferi obtained from North America and Europe has demonstrated that OspA has antigenic variability, and that several distinct groups can be serologically and genotypically defined (Wilske, B., et al., World J. Microbiol. 7: 130 (1991)). Other Borrelia proteins 10 demonstrate similar antigenic variability. Surprisingly, the immune response to these outer surface proteins tends to occur late in the disease, if at all (Craft, J. E. et al., J. Clin Invest. 78: 934-939 (1986); Dattwyler, R.J. and B.J. Luft, Rheum. Clin. 15 North Am. 15: 727-734 (1989)). Furthermore, patients acutely and chronically infected with B. burgdorferi respond variably to the different antigens, including OspA, OspB, OspC, OspD, p39, p41 and p93.

Vaccines against Lyme borreliosis have been attempted. Mice immunized with a recombinant form of OspA are protected from challenge with the same strain of B. burgdorferi from which the protein was obtained (Fikrig, E., et al., Science 250: 553-556 (1990)). Furthermore, passively transferred anti-OspA monoclonal

antibodies (Mabs) have been shown to be protective in mice, and vaccination with a recombinant protein induced protective immunity against subsequent infection with the homologous strain of B.burgdorferi (Simon, M.M., et

al., <u>J. Infect. Dis. 164</u>: 123 (1991)). Unfortunately, immunization with a protein from one strain does not necessarily confer resistance to a heterologous strain (Fikrig, E. et al., <u>J. Immunol. 7</u>: 2256-1160 (1992)), but rather, is limited to the homologous 'species' from which the protein was prepared. Furthermore,

immunization with a single protein from a particular strain of Borrelia will not confer resistance to that strain in all individuals. There is considerable variation displayed in OspA and OspB, as well as p93, including the regions conferring antigenicity.

Therefore, the degree and frequency of protection from vaccination with a protein from a single strain depend upon the response of the immune system to the particular variation, as well as the frequency of genetic variation in B. burgdorferi. Currently, a need exists for a vaccine which provides immunogenicity across species and to more epitopes within a species, as well as immunogenicity against more than one protein.

Summary of the Invention

The current invention pertains to chimeric Borrelia proteins which include two or more antigenic Borrelia polypeptides which do not occur naturally (in nature) in the same protein in Borrelia, as well as the nucleic acids encoding such chimeric proteins. The antigenic polypeptides incorporated in the chimeric proteins are derived from any Borrelia protein from any strain of Borrelia, and include outer surface protein (Osp) A, OspB, OspC, OspD, p12, p39, p41, p66, and p93. proteins from which the antigenic polypeptides are 25 derived can be from the same strain of Borrelia, from different strains, or from combinations of proteins from the same and from different strains. If the proteins from which the antigenic polypeptides are derived are OspA or OspB, the antigenic polypeptides can be derived 30 from either the portion of the OspA or OspB protein present between the amino terminus and the conserved tryptophan of the protein (referred to as a proximal portion), or the portion of the OspA or OspB protein present between the conserved tryptophan of the protein

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and the carboxy terminus (referred to as a distal portion). Particular chimeric proteins, and the nucleotide sequences encoding them, are set forth in Figures 23-37 and 43-46.

The chimeric proteins of the current invention provide antigenic polypeptides of a variety of Borrelia strains and/or proteins within a single protein. Such proteins are particularly useful in immunodiagostic assays to detect the presence of antibodies to native Borrelia in potentially infected individuals as well as to measure T-cell reactivity, and can therefore be used as immunodiagnostic reagents. The chimeric proteins of the current invention are additionally useful as vaccine immunogens against Borrelia infection.

For a better understanding of the present invention together with other and further objects, reference is made to the following description, taken together with the accompanying drawings.

Brief Description of the Drawings

Figure 1 summarizes peptides and antigenic domains localized by proteolytic and chemical fragmentation of OspA.

Figure 2 is a comparison of the antigenic domains depicted in Figure 1, for OspA in nine strains of B. burgdorferi.

Figure 3 is a graph depicting a plot of weighted polymorphism versus amino acid position among 14 OspA variants. The marked peaks are: a) amino acids 132-145; b) amino acids 163-177; c) amino acids 208-221. The lower dotted line at polymorphism value 1.395 demarcates statistically significant excesses of polymorphism at p = 0.05. The upper dotted line at 1.520 is the same, except that the first 29 amino acids at the monomorphic N-terminus have been removed from the original analysis.

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Figure 4 depicts the amino acid alignment of residues 200 through 220 for OspAs from strains B31 and K48 as well as for the site-directed mutants 613, 625, 640, 613/625, and 613/640. Arrow indicates Trp216.

5 Amino acid changes are underlined.

Figure 5 is a helical wheel projection of residues 204-217 of B31 OspA. Capital letters indicate hydrophobic residues; lower case letters indicate hydrophilic residues; +/- indicate positively/negatively charged residues. Dashed line indicates division of the alpha-helix into hydrophobic arc (above the line) and polar arc (below the line). Adapted from France et al. (Biochem. Biophys. Acta 1120: 59 (1992)).

Figure 6 depicts a phylogenic tree for strains of Borrelia described in Table I. The strains are as follows: 1 = B31; 2 = Pka1; 3 = ZS7; 4 = N40; 5 = 25015; 6 = K48; 7 = DK29; 8 = PHei; 9 = Ip90; 10 = PTrob; 11 = ACAI; 12 = PGau; 13 = Ip3; 14 = PBo; 15 = PKo.

Figure 7 depicts the nucleic acid sequence of OspA-B31 (SEW ID NO. 6), and the encoded protein sequence (SEQ ID NO. 7).

Figure 8 depicts the nucleic acid sequence of OspA-K48 (SEQ ID NO. 8), and the encoded protein sequence (SEQ ID NO. 9).

Figure 9 depicts the nucleic acid sequence of OspA-PGau (SEQ ID NO. 10), and the encoded protein sequence (SEQ ID NO. 11).

Figure 10 depicts the nucleic acid sequence of 30 OspA-25015 (SEQ ID NO. 12), and the encoded protein sequence (SEQ ID NO. 13).

Figure 11 depicts the nucleic acid sequence of OspB-B31 (SEQ ID NO. 21), and the encoded protein sequence (SEQ ID NO. 22).

Figure 12 depicts the nucleic acid sequence of OspC-B31 (SEQ ID NO. 29), and the encoded protein sequence (SEQ ID NO. 30).

Figure 13 depicts the nucleic acid sequence of OspC-K48 (SEQ ID NO. 31), and the encoded protein sequence (SEQ ID NO. 32).

Figure 14 depicts the nucleic acid sequence of OspC-PKo (SEQ ID NO. 33), and the encoded protein sequence (SEQ ID NO. 34).

10 Figure 15 depicts the nucleic acid sequence of OspC-pTrob (SEQ ID NO. 35) and the encoded protein sequence (SEQ ID NO. 36).

Figure 16 depicts the nucleic acid sequence of p93-B31 (SEQ ID NO. 65) and the encoded protein sequence (SEQ ID NO. 66).

Figure 17 depicts the nucleic acid sequence of p93-K48 (SEQ ID NO. 67).

Figure 18 depicts the nucleic acid sequence of p93-PBo (SEQ ID NO. 69).

20 Figure 19 depicts the nucleic acid sequence of p93-pTrob (SEQ ID NO. 71).

Figure 20 depicts the nucleic acid sequence of p93-pGau (SEQ ID NO. 73).

Figure 21 depicts the nucleic acid sequence of p93-25 25015 (SEQ ID NO. 75).

Figure 22 depicts the nucleic acid sequence of p93pKo (SEQ ID NO. 77).

Figure 23 depicts the nucleic acid sequence of the OspA-K48/OspA-PGau chimer (SEQ ID NO. 85) and the encoded chimeric protein sequence (SEQ ID NO. 86).

Figure 24 depicts the nucleic acid sequence of the OspA-B31/OspA-PGau chimer (SEQ ID NO. 88) and the encoded chimeric protein sequence (SEQ ID NO. 89).

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Figure 25 depicts the nucleic acid sequence of the OspA-B31/OspA-K48 chimer (SEQ ID NO. 91) and the encoded chimeric protein sequence (SEQ ID NO. 92).

Figure 26 depicts the nucleic acid sequence of the OspA-B31/OspA-25015 chimer (SEQ ID NO. 94) and the encoded chimeric protein sequence (SEQ ID NO. 95).

Figure 27 depicts the nucleic acid sequence of the OspA-K48/OspA-B31/OspA-K48 chimer (SEQ ID NO. 97) and the encoded chimeric protein sequence (SEQ ID NO. 98).

Figure 28 depicts the nucleic acid sequence of the OspA-B31/OspA-K48/OspA-B31/OspA-K48 chimer (SEQ ID NO. 100) and the encoded chimeric protein sequence (SEQ ID NO. 101).

Figure 29 depicts the nucleic acid sequence of the OspA-B31/OspB-B31 chimer (SEQ ID NO. 103) and the encoded chimeric protein sequence (SEQ ID NO. 104).

Figure 30 depicts the nucleic acid sequence of the OspA-B31/OspB-B31/OspC-B31 chimer (SEQ ID NO. 106) and the encoded chimeric protein sequence (SEQ ID NO. 107).

Figure 31 depicts the nucleic acid sequence of the OspC-B31/OspA-B31/OspB-B31 chimer (SEQ ID NO. 109) and the encoded chimeric protein sequence (SEQ ID NO. 110).

Figure 32 depicts the nucleic acid sequence of the OspA-B31/p93-B31 chimer (SEQ ID NO. 111) and the encoded chimeric protein sequence (SEQ ID NO. 112).

Figure 33 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (122-234) chimer (SEQ ID NO. 113) and the encoded chimeric protein sequence (SEQ ID NO. 114).

Figure 34 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (122-295) chimer (SEQ ID NO. 115) and the encoded chimeric protein sequence (SEQ ID NO. 116).

Figure 35 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (140-234) chimer (SEQ ID NO. 117) and the encoded chimeric protein sequence (SEQ ID NO. 118).

Figure 36 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (140-295) chimer (SEQ ID NO. 119) and the encoded chimeric protein sequence (SEQ ID NO. 120).

Figure 37 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (122-234)/OspC-B31 chimer (SEQ ID NO. 121) and the encoded chimeric protein sequence (SEQ ID NO. 122).

Figure 38 depicts an alignment of the nucleic acid sequences for OspC-B31 (SEQ ID NO. 29), OspC-PKo (SEQ ID NO. 33), OspC-pTrob (SEQ ID NO. 35), and OspC-K48 (SEQ ID NO. 31). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspC-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 39 depicts an alignment of the nucleic acid sequences for OspD-pBO (SEQ ID NO. 123), OspD-pGau (SEQ ID NO. 124), OspD-DK29 (SEQ ID NO. 125), and OspD-K48 (SEQ ID NO. 126). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspD-pBo) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 40 depicts the nucleic acid sequence of p41-B31 (SEq ID NO. 127) and then encoded protein sequence (SEQ ID NO. 128).

Figure 41 depicts an alignment of the nucleic acid sequences for p41-B31 (SEQ ID NO. 127), p41-pKa1 (SEQ ID NO. 129), p41-PGau (SEQ ID NO. 51), p41-PBo (SEQ ID NO. 130), p41-DK29 (SEQ ID NO. 53), and p41-PKo (SEQ ID NO. 131). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, p41-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 42 depicts an alignment of the nucleic acid sequences for OspA-B31 (SEQ ID NO. 6), OspA-pKa1 (SEQ ID NO. 132), OspA-N40 (SEQ ID NO. 133), OspA-ZS7 (SEQ ID

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NO. 134), OspA-25015 (SEQ ID NO. 12), OspA-pTrob (SEQ ID NO. 135), OspA-K48 (SEQ ID NO. 8), OspA-Hei (SEQ ID NO. 136), OspA-DK29 (SEQ ID NO. 49), OSpA-Ip90 (SEQ ID NO. 50), OspA-pBo (Seq ID NO. 55), OspA-Ip3 (SEQ ID NO. 56), OspA-PKo (SEQ ID NO. 57), OspA-ACAI (SEQ ID NO. 58), and OspA-PGau (SEQ ID NO. 10). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspA-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 43 depicts the nucleic acid sequence of the OspA-Tro/OspA-Bo chimer (SEQ ID NO. 137) and the encoded chimeric protein sequence (SEQ ID NO. 138).

Figure 44 depicts the nucleic acid sequence of the OspA-PGau/OspA-Bo chimer (SEQ ID NO. 139) and the encoded chimeric protein sequence (SEQ ID NO. 140).

Figure 45 depicts the nucleic acid sequence of the OspA-B31/OspA-PGau/OspA-B31/OspA-K48 chimer (SEQ ID NO. 141) and the encoded chimeric protein sequence (SEQ ID NO. 142).

Figure 46 depicts the nucleic acid sequence of the OspA-PGau/OspA-B31/OspA-K48 chimer (SEQ ID NO. 143) and the encoded chimeric protein sequence (SEQ ID NO. 144).

Detailed Description of the Invention

The current invention pertains to chimeric proteins
comprising antigenic Borrelia polypeptides which do not
occur in nature in the same Borrelia protein. The
chimeric proteins are a combination of two or more
antigenic polypeptides derived from Borrelia proteins.
The antigenic polypeptides can be derived from different
proteins from the same species of Borrelia, or different
proteins from different Borrelia species, as well as
from corresponding proteins from different species. As
used herein, the term "chimeric protein" describes a
protein comprising two or more polypeptides which are

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derived from corresponding and/or non-corresponding native Borrelia protein. A polypeptide "derived from" a native Borrelia protein is a polypeptide which has an amino acid sequence the same as an amino acid sequence present in a Borrelia protein, an amino acid sequence equivalent to the amino acid sequence of a naturally occurring Borrelia protein, or an amino acid sequence substantially similar to the amino acid sequence of a naturally occurring Borrelia protein (e.g., differing by few amino acids) such as when a nucleic acid encoding a protein is subjected to site-directed mutagenesis. "Corresponding" proteins are equivalent proteins from different species or strains of Borrelia, such as outer surface protein A (OspA) from strain B31 and OspA from strain K48. The invention additionally pertains to nucleic acids encoding these chimeric proteins.

As described below, Applicants have identified two separate antigenic domains of OspA and OspB which flank the sole conserved tryptophan present in OspA and in These domains share cross-reactivity with different genospecies of Borrelia. The precise amino acids responsible for antigenic variability were determined through site-directed mutagenesis, so that proteins with specific amino acid substitutions are available for the development of chimeric proteins. Furthermore, Applicants have identified immunologically important hypervariable domains in OspA proteins, as described below in Example 2. The first hypervariable domain of interest for chimeric proteins, Domain A, 30 includes amino acid residues 120-140 of OspA, the second hypervariable domain, Domain B, includes residues 150-180 and the third hypervariable domain, Domain C, includes residues 200-216 or 217 (depending on the position of the sole conserved tryptophan residue in the OspA of that particular species of Borrelia) (see Figure 3). In addition, Applicants have sequenced the genes for several *Borrelia* proteins.

These discoveries have aided in the development of novel recombinant Borrelia proteins which include two or more amino acid regions or sequences which do not occur in the same Borrelia protein in nature. The recombinant proteins comprise polypeptides from a variety of Borrelia proteins, including, but not limited to, OspA, OspB, OspC, OspD, p12, p39, p41, p66, and p93.

10 Antigenically relevant polypeptides from each of a number of proteins are combined into a single chimeric protein.

In one embodiment of the current invention, chimers are now available which include antigenic polypeptides 15y flanking a tryptophan residue. The antigenic polypeptides are derived from either the proximal portion from the tryptophan (the portion of the OspA or OspB protein present between the amino terminus and the conserved tryptophan of the protein), or the distal portion from the tryptophan (the portion of the OspA or OspB protein present between the conserved tryptophan of the protein and the carboxy terminus) in OspA and/or The resultant chimers can be OspA-OspA chimers (i.e., chimers incorporating polypeptides derived from OspA from different strains of Borrelia), OspA-OspB 25 chimers, or OspB-OspB chimers, and are constructed such that amino acid residues amino-proximal to an invariant tryptophan are from one protein and residues carboxyproximal to the invariant tryptophan are from the other protein. For example, one available chimer consists of a polypeptide derived from the amino-proximal region of OspA from strain B31, followed by the tryptophan residue, followed by a polypeptide derived from the carboxy-proximal region of OspA from strain K48 (SEQ ID

35 NO. 92). Another available chimer includes a

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polypeptide derived from the amino-proximal region of OspA from strain B31, and a polypeptide derived from the carboxy-proximal region of OspB from strain B31 (SEQ ID NO. 104). If the polypeptide proximal to the tryptophan 5 of these chimeric proteins is derived from OspA, the proximal polypeptide can be further subdivided into the three hypervariable domains (Domains A, B, and C), each of which can be derived from OspA from a different These chimeric proteins can further strain of Borrelia. comprise antigenic polypeptides from another protein, in addition to the antigenic polypeptides flanking the tryptophan residue.

In another embodiment of the current invention, chimeric proteins are available which incorporate antigenic domains of two or more Borrelia proteins, such as Osp proteins (Osp A, B, C and/or D) as well as p12, p39, p41, p66, and/or p93.

The chimers described herein can be produced so that they are highly soluble, hyper-produced in E. coli, and non-lipidated. In addition, the chimeric proteins can be designed to end in an affinity tag (His-tag) to facilitate purification. The recombinant proteins described herein have been constructed to maintain high levels of antigenicity. In addition, recombinant proteins specific for the various genospecies of Borrelia that cause Lyme disease are now available, because the genes from each of the major genospecies have been sequenced; the sequences are set forth below. These recombinant proteins with their novel biophysical and antigenic properties will be important diagnostic reagent and vaccine candidates.

The chimeric proteins of the current invention are advantageous in that they retain specific reactivity to monoclonal and polyclonal antibodies against wild-type Borrelia proteins, are immunogenic, and inhibit the

growth or induce lysis of Borrelia in vitro.

Furthermore, in some embodiments, the proteins provide antigenic domains of two or more Borrelia strains and/or proteins within a single protein. Such proteins are

5 particularly useful in immuno-diagostic assays. For example, proteins of the present invention can be used as reagents in assays to detect the presence of antibodies to native Borrelia in potentially infected individuals. These proteins can also be used as

10 immunodiagnostic reagents, such as in dot blots, Western blots, enzyme linked immunosorbed assays, or agglutination assays. The chimeric proteins of the present invention can be produced by known techniques, such as by recombinant methodology, polymerase chain

15 reaction, or mutagenesis.

Furthermore, the proteins of the current invention are useful as vaccine immunogens against Borrelia infection. Because Borrelia has been shown to be clonal, a protein comprising antigenic polypeptides from 20 a variety of Borrelia proteins and/or species, will provide immunoprotection for a considerable time when used in a vaccine. The lack of significant intragenic recombination, a process which might rapidly generate novel epitopes with changed antigenic properties, 25 ensures that Borrelia can only change antigenic type by accumulating mutational change, which is slow when compared with recombination in generating different The chimeric protein can be combined antigenic types. with a physiologically acceptable carrier and 30 administered to a vertebrate animal through standard methods (e.g., intravenously or intramuscularly, for example).

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The current invention is illustrated by the following Examples, which are not to be construed to be limiting in any way.

Example 1. Purification of Borrelia burgorferi Outer Surface Protein A and Analysis of Antibody Binding Domains

This example details a method for the purification of large amounts of native outer surface protein A (OspA) to homogeneity, and describes mapping of the antigenic specificities of several anti-OspA MAbs. OspA was purified to homogeneity by exploiting its resistance to trypsin digestion. Intrinsic labeling with ¹⁴C-palmitic acid confirmed that OspA was lipidated, and partial digestion established lipidation at the aminoterminal cysteine of the molecule.

The reactivity of seven anti-OspA murine monoclonal antibodies to nine different Borrelia isolates was ascertained by Western blot analysis. Purified OspA was fragmented by enzymatic or chemical cleavage, and the monoclonal antibodies were able to define four distinct immunogenic domains (see Figure 1). Domain 3, which included residues 190-220 of OspA, was reactive with protective antibodies known to agglutinate the organism in vitro, and included distinct specificities, some of which were not restricted to a genotype of B. burgdorferi.

A. Purification of Native OspA

Detergent solubilization of B. burgdorferi strips the outer surface proteins and yields partially-purified preparations containing both OspA and outer surface 5 protein B (Osp B) (Barbour, A.G. et al., Infect. Immun. 52 (5): 549-554 (1986); Coleman, J.L. and J.L. Benach, J Infect. Dis. 155 (4): 756-765 (1987); Cunningham, T.M. et al., Ann. NY Acad. Sci. 539: 376-378 (1988); Brandt, M.E. et al., <u>Infect. Immun. 58</u>: 983-991 (1990); Sambri, 10 V. and R. Cevenini, Microbiol. 14:307-314 (1991)). Although both OspA and OspB are sensitive to proteinase K digestion, in contrast to OspB, OspA is resistant to cleavage by trypsin (Dunn, J. et al., Prot. Exp. Purif. 1: 159-168 (1990); Barbour, A.G. et al., <u>Infect. Immun.</u> 15 45:94-100 (1984)). The relative insensitivity to trypsin is surprising in view of the fact that Osp A has a high (16% for B31) lysine content, and may relate to the relative configuration of Osp A and B in the outer membrane.

Intrinsic Radiolabeling of Borrelia

Labeling for lipoproteins was performed as described by Brandt et al. (Infect. Immun. 58:983-991 (1990)). ¹⁴C-palmitic acid (ICN, Irvine, California) was added to the BSK II media to a final concentration of 0.5 μCi per milliliter (ml). Organisms were cultured at 34°C in this medium until a density of 10⁸ cells per ml was achieved.

Purification of OspA Protein from Borrelia Strain B31

Borrelia burgdorferi, either 14C-palmitic acidlabeled or unlabeled, were harvested and washed as
described (Brandt, M.E. et al., Infect. Immun. 58:983991 (1990)). Whole organisms were trypsinized according

to the protocol of Barbour et al. (Infect. Immun. 45:94-100 (1984)) with some modifications. The pellet was suspended in phosphate buffered saline (PBS, 10mM, pH 7.2), containing 0.8% tosyl-L-phenylalanine chloromethyl ketone (TPCK)-treated trypsin (Sigma, St. Louis, Missouri), the latter at a ratio of 1 μ g per 108 cells. Reaction was carried out at 25°C for 1 hour, following which the cells were centrifuged. The pellet was washed in PBS with 100 μ g/ml phenylmethylsulfonyl fluoride Triton X-114 partitioning of the pellet was 10 carried out as described by Brandt et al. (Infect. Immun. 58:983-991 (1990)). Following trypsin treatment, cells were resuspended in ice-cold 2% (v/v) Triton X-114 in PBS at 109 cells per ml. The suspension was rotated overnight at 4°C, and the insoluble fraction removed as a pellet after centrifugation at 10,000 X g for 15 minutes at 4°C. The supernatant (soluble fraction) was incubated at 37°C for 15 minutes and centrifuged at room temperature at 1000 X g for 15 minutes to separate the aqueous and detergent phases. The aqueous phase was decanted, and ice cold PBS added to the lower Triton phase, mixed, warmed to 37°C, and again centrifuged at 1000 X g for 15 minutes. Washing was repeated twice more. Finally, detergent was removed from the preparation using a spin column of Bio-beads SM2 (BioRad, Melville, New York) as described (Holloway, P.W., Anal. Biochem. 53:304-308 (1973)).

Ion exchange chromatography was carried out as described by Dunn et al. (Prot. Exp. Purif. 1: 159-168 (1990)) with minor modifications. Crude OspA was dissolved in buffer A (1% Triton X-100, 10mM phosphate buffer (pH 5.0)) and loaded onto a SP Sepharose resin (Pharmacia, Piscataway, New Jersey), pre-equilibrated with buffer A at 25°C. After washing the column with 10

bed-volumes of buffer A, the bound OspA was eluted with buffer B (1% Triton X-100, 10mM phosphate buffer (pH 8.0)). OspA fractions were detected by protein assay using the BCA method (Pierce, Rockford, Illinois), or as radioactivity when intrinsically labeled material was fractionated. Triton X-100 was removed using a spin column of Bio-beads SM2.

This method purifies OspA from an outer surface membrane preparation. In the absence of trypsin
treatment, OspA and B were the major components of the soluble fraction obtained after Triton partitioning of strain B31. In contrast, when Triton extraction was carried out after trypsin-treatment, the OspB band is not seen. Further purification of OspA-B31 on a SP

Sepharose column resulted in a single band by SDS-PAGE. The yield following removal of detergent was approximately 2 mg per liter of culture. This method of purification of OspA, as described herein for strain B31, can be used for other isolates of Borrelia as well.

For strains such as strain K48, which lack OspB, trypsin treatment can be omitted.

Lipidation site of OspA-B31

¹⁴C-palmitic acid labeled OspA from strain B31 was purified as described above and partially digested with endoproteinase Asp-N (data not shown). Following digestion, a new band of lower molecular weight was apparent by SDS-PAGE, found by direct amino-terminal sequencing to begin at Asp₂₅. This band had no trace of radioactivity by autoradiography (data not shown). OspA and B contain a signal sequence (L-X-Y-C) similar to the consensus described for lipoproteins of E. coli, and it has been predicted that the lipidation site of OspA and B should be the amino-terminal cysteine (Brandt, M.E. et

al., <u>Infect. Immun 58</u>: 983-991 (1990)). The results presented herein support this prediction.

B. Comparison of OspA Antibody Binding Regions in Nine Strains of Borrelia burgdorferi

The availability of the amino acid sequenced for OspA from a number of different isolates, combined with peptide mapping and Western blot analysis, permitted the identification of the antigenic domains recognized by monoclonal antibodies (MAbs) and allowed inference of the key amino acid residues responsible for specific antibody reactivity.

Strains of Borrelia burgdorferi

Nine strains of *Borrelia*, including seven European strains and two North American strains, were used in this study of antibody binding domains of several proteins. Information concerning the strains is summarized in Table I, below.

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Table I. Representative Borrelia Strains

Strain		
	Location and Source	Reference for Strain
K48	Czechoslovakia, Ixodes ricinus	none .
PGau	Germany, human ACA	Wilske, B. et al., <u>J. Clin.</u> <u>Microbiol. 32</u> :340-350 (1993)
DK29	Denmark, human EM	Wilske, B. et al.
PKo	Germany, human EM	Wilske, B. et al.
PTrob	Germany, human skin	Wilske, B. et al.
Ip3	Khabarovsk, Russia, I. persulcatus	Asbrink, E. <i>et al.</i> , <u>Acta</u> <u>Derm. Venereol. 64</u> : 506-512 (1984)
Ip90	Khabarovsk, Russia, I. persulcatus	Asbrink, E. et al.
25015	Millbrook, NY, I. persulcatus	Barbour, A.G. et al., <u>Curr.</u> <u>Microbiol. 8</u> :123-126 (1983)
B31	Shelter Island, NY, I. scapularis	Luft, B.J. et al., <u>Infect.</u> <u>Immun. 60</u> : 4309-4321 (1992); ATCC 35210
PKa1	Germany, human CSF	Wilske, B. et al.
ZS7	Freiburg, Germany, I. ricinus	Wallich, R. <i>et al.</i> , <u>Nucl.</u> <u>Acids Res. 17</u> : 8864 (1989)
N40	Westchester Co., NY	Fikrig, E. et al., <u>Science</u> <u>250</u> :553-556 (1990)
PHei	Germany, human CSF	Wilske, B. et al.
ACAI	Sweden, human ACA	Luft, B. J. et al., <u>FEMS</u> <u>Microbiol. Lett. 93</u> :73-68 (1992)
PBo	Germany, human CSF	Wilske, B. et al.

ACA = patient with acrodermatitis chronica atrophicans; EM = patient with erythema migrans; CSF = cerebrospinal fluid of patient with Lyme disease

Strains K48, PGau and DK29 were supplied by R. Johnson, University of Minnesota; PKo and pTrob were provided by B. Wilske and V. Preac-Mursic of the

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Pettenkhofer Institute, Munich, Germany; and Ip3 and Ip90 were supplied by L. Mayer of the Center for Disease Control, Atlanta, Georgia. The North American strains included strain 25015, provided by J. Anderson of the Connecticut Department of Agriculture; and strain B31 (ATCC 35210).

Monoclonal Antibodies

Seven monoclonal antibodies (MAbs) were utilized in this study. Five of the MAbs (12, 13, 15, 83 and 336) were produced from hybridomas cloned and subcloned as previously 10 described (Schubach, W.H., et al., Infect. Immun. 59(6):1911-1915 (1991)). MAb H5332 (Barbour, A.G. et al., Infect. Immun. 41:795-804 (1983)) was a gift from Drs. Alan Barbour, University of Texas, and MAb CIII.78 (Sears, J.E. et al., J. Immunol. 147(6):1995-2000 (1991)) was a gift 15 from Richard A. Flavell, Yale University. MAbs 12 and 15 were raised against whole sonicated B3; MAb 336 was produced against whole PGau; and MAbs 13 and 83 were raised to a truncated form of OspA cloned from the K48 strain and expressed in E. coli using the T7 RNA polymerase system 20 (McGrath, B.C. et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York, pp. 365-370 (1993)). All MAbs were typed as being Immunoglobulin G (IgG).

Methods of Protein Cleavage, Western Blotting, and Amino-Terminal Sequencing

Prediction of the various cleavage sites was achieved by knowledge of the primary amino acid sequence derived from the full nucleotide sequences of OspA, many of which are currently available (see Table II, below). Cleavage sites can also be predicted based on the peptide sequence of OspA, which can be determined by standard techniques after isolation and purification of OspA by the method described above. Cleavage of several OspA isolates was

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conducted to determine the localization of monoclonal antibody binding of the proteins.

Hydroxylamine-HCl (HA), N-chlorosuccinimide (NCS), and cyanogen bromide cleavage of OspA followed the methods

5 described by Bornstein (Biochem. 9 (12):2408-2421 (1970)), Shechter et al., (Biochem. 15 (23):5071-5075 (1976)), and Gross (in Hirs, C.H.W. (ed): Methods in Enzymology, (N.Y. Acad. Press), 11:238-255 (1967)) respectively. Protease cleavage by endoproteinase, Asp-N (Boehringer Mannheim,

10 Indianapolis, Indiana), was performed as described by Cleveland D.W. et al., (J. Biol. Chem. 252:1102-1106 (1977)). Ten micrograms of OspA were used for each reaction. The ratio of enzyme to OspA was approximately 1 to 10 (w/w).

- Proteins and peptides generated by cleavage were separated by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) (Laemmli, U.K., Nature (London) 227:680-685 (1970)), and electroblotted onto immobilon Polyvinylidine Difluoride (PVDF) membranes (Ploskal, M.G. et al., Biotechniques
- 20 4:272-283 (1986)). They were detected by amido black staining or by immunostaining with murine MAbs, followed by alkaline phosphatase-conjugated goat antimouse IgG. Specific binding was detected using a 5-bromo-4-chloro-3-indolylphosphate (BCIP)/nitroblue tetrazolium (NBT)
 25 developer system (KPL Inc. Gathersburg, Maryland)
- 25 developer system (KPL Inc., Gathersburg, Maryland).

 In addition, amino-terminal amino acid sequence
 analysis was carried out on several cleavage products, as
 described by Luft et al. (Infect. Immun. 57:3637-3645
 (1989)). Amido black stained bands were excised from PVDF
- 30 blots and sequenced by Edman degradation using a Biosystems model 475A sequenator with model 120A PTH analyzer and model 900A control/data analyzer.

Cleavage Products of Outer Surface Protein A Isolates Purified OspA-B31, labeled with 14C-palmitic acid, was fragmented with hydroxylamine-HCl (HA) into two peptides, designated HA1 and HA2 (data not shown). The HA1 band migrated at 27 KD and retained its radioactivity, indicating that the peptide included the lipidation site at the N-terminus of the molecule (data not shown). From the predicted cleavage point, HA1 should correspond to residues 1 to 251 of OspA-B31. HA2 had a MW of 21.6 KD by SDS-PAGE, 10 with amino-terminal sequence analysis showing it to begin at Gly72, i.e. residues 72 to 273 of OspA-B31. By contrast, HA cleaved OspA-K48 into three peptides, designated HA1, HA2, and HA3 with apparent MWs of 22KD, 16 KD and 12 KD, respectively. Amino-terminal sequencing 15 showed HA1 to start at Gly72, and HA3 at Gly142. found to have a blocked amino-terminus, as was observed for the full-length OspA protein. HA1, 2 and 3 of OspA-K48 were predicted to be residues 72-274, 1 to 141 and 142 to 274, respectively.

N-Chlorosuccinimide (NCS) cleaves tryptophan (W), which is at residue 216 of OspA-B31 or residue 217 of OspA-K48 (data not shown). NCS cleaved OspA-B31 into 2 fragments, NCS1, with MW of 23 KD, residues 1-216 of the protein, and NCS2 with a MW of 6.2 KD, residues 217 to 273 (data not shown). Similarly, K48 OspA was divided into 2 pieces, NCS1 residues 1-217, and NCS2 residues 218 to 274 (data not shown).

Cleavage of OspA by cyanogen bromide (CNBr) occurs at the carboxy side of methionine, residue 39. The major fragment, CNBr1, has a MW of 25.7 KD, residues 39-274 by amino-terminal amino acid sequence analysis (data not shown). CNBr2 (about 4 KD) could not be visualized by amido black staining; instead, lightly stained bands of about 20 KD MW were seen. These bands reacted with anti-

OspA MAbs, and most likely were degradation products due to cleavage by formic acid.

Determination of Antibody Binding Domains for Anti-OspA Monoclonal Antibodies

The cleavage products of OspA-B31 and OspA-K48 were analyzed by Western blot to assess their ability to bind to the six different MAbs. Preliminary Western blot analysis of the cleavage products demonstrated that strains K48 and DK29 have similar patterns of reactivity, as do IP3, PGau

and PKo. The OspA of strain PTrob was immunologically distinct from the others, being recognized only by MAb 336. MAb 12 recognized only the two North American strains, B31 and 25015. When the isolates were separated into genogroups, it was remarkable that all the MAbs, except MAb 12, crossed over to react with multiple genogroups.

MAb12, specific for OspA-B31, bound to both HA1 and HA2 of OspA-B31. However, cleavage of OspA-B31 by NCS at residue Trp216 created fragments which did not react with MAb12, suggesting that the relevant domain is near or is structurally dependent upon the integrity of this residue (data not shown). MAb 13 bound only to OspA-K48, and to peptides containing the amino-terminus of that molecule (e.g. HA2; NCS1). It did not bind to CNBr1 residues 39 to 274. Thus the domain recognized by MAb13 is in the amino-terminal end of OspA-K48, near Met38.

MAb15 reacts with the OspA of both the B31 and K48 strains, and to peptides containing the N-terminus of OspA, such as HA1 of OspA-B31 and NCS1, but not to peptides HA2 of OspA-B31 and HA1 of OspA-K48 (data not shown). Both peptides include residue 72 to the C-terminus of the molecules. MAb15 bound to CNBr1 of OspA-K48, indicating the domain for this antibody to be residues 39 to 72, specifically near Gly72 (data not shown).

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MAD83 binds to OspA-K48, and to peptides containing the C-terminal portion of the molecule, such as HA1. They do not bind to HA2 of OspA-K48, most likely because the C-terminus of HA2 of OspA-K48 ends at 141. Similar to MAb12 and OspA-B31, binding of MAbs 83 and CIII.78 is eliminated by cleavage of OspA at the tryptophan residue. Thus binding of MAbs 12, 83 and CIII.78 to OspA depends on the structural integrity of the Trp216 residue, which appears to be critical for antigenicity. Also apparent is that, although these MAbs bind to a common antigenic domain, the precise epitopes which they recognize are distinct from one another given the varying degrees of cross-reactivity to these MAbs among strains.

Although there is similar loss of binding activity of 15 MAb336 with cleavage at Trp216, this MAb does not bind to HA1 of OspA-B31, suggesting the domain for this antibody includes the carboxy-terminal end of the molecule, inclusive of residues 251 to 273. Low MW peptides, such as HA3 (10 KD) and NCS2 (6KD), of OspA-K48 do not bind this MAb on Western blots. In order to confirm this 20 observation, we tested binding of the 6 MAbs with a recombinant fusion construct p3A/EC that contains a trpE leader protein fused with residues 217 to 273 of OspA-B31 (Schubach, W.H. et al., <u>Infect. Immun. 59(6)</u>: 1911-1915 (1991)). Only MAb336 reacted with this construct (data not 25 shown). Peptides and antigenic domains localized by fragmentation of OspA are summarized in Figure 1.

Mapping of Domains to Define the Molecular Basis for the Serotype Analysis

To define the molecular basis for the serotype analysis of OspA, we compared the derived amino acid sequences of OspA for the nine isolates (Figure 2). At the amino terminus of the protein, these predictions can be more precise given the relatively small number of amino

acid substitutions in this region compared to the carboxy terminus. Domain 1, which is recognized by MAb13, includes residues Leu34 to Leu41. MAb13 only binds to the OspA of species K48, DK29 and IP90. Within this region, residue 37 5 is variable, however Gly37 is conserved amongst the three reactive strains. When Gly37 is changed to Glu37, as it is in OspA of strains B31, pTrob, PGau, and PKo, MAb13 does not recognize the protein (data not shown). By similar analysis, it can be seen that Asp70 is a crucial residue 10 for Domain 2, which includes residues 65 to 75 and is recognized by MAb15. Domain 3 is reactive with MAbs H5332, 12 and 83, and includes residues 190-220. It is clear that significant heterogeneity exists between MAbs reactive with this domain, and that more than one conformational epitope 15 must be contained within the sequence. Domain 4 binds MAb336, and includes residues 250 to 270. In this region, residue 266 is variable and therefore may be an important determinant. It is apparent, however, that other determinants of the reactivity of this monoclonal antibody 20 reside in the region comprising amino acids 217-250. Furthermore, the structural integrity of Trp216 is essential for antibody reactivity in the intact protein. Finally, it is important to stress that Figure 2 indicates only the locations of the domains, and does not necessarily 25 encompass the entire domain. Exact epitopes are being analyzed by site-directed mutagenesis of specific residues.

Overall, evidence suggests that the N-terminal portion is not the immunodominant domain of OspA, possibly by virtue of its lipidation, and the putative function of the lipid moiety in anchoring the protein to the outer envelope. The C-terminal end is immunodominant and includes domains that account in part for structural heterogeneity (Wilske, B. et al., Med. Microbiol. Immunol. 181: 191-207 (1992)), and may provide epitopes for antibody

neutralization (Sears, J.E. et al., J. Immunol. 147(6):
1995-2000 (1991)), and relate to other activities, such as
the induction of T-cell proliferation (Shanafel, M.M., et
al., J. Immunol. 148: 218-224 (1992)). There are common
epitopes in the carboxy-end of the protein that are shared
among genospecies which may have immunoprotective potential
(Wilske, B., et al., Med. Microbiol. Immunol. 181: 191-207
(1992)).

Prediction of secondary structure on the basis of

hydropathy analysis and circular dichroism and fluorescence
spectroscopy measurements (McGrath, B.C., et al., Vaccines,
Cold Spring Harbor Laboratory Press, Plainview, New York;
pp. 365-370 (1993)) suggest domains 3 and 4 to be in a
region of the molecule with a propensity to form alphahelix, whereas domains 1 and 2 occur in regions predicted
to be beta-sheets (see Figure 1). These differences may
distinguish domains in accessibility to antibody or to
reactive T-cells (Shanafel, M.M. et al., J. Immunol. 148:
218-224 (1992)). Site-directed mutagenesis of specific
epitopes, as described below in Example 2, aids in
identifying exact epitopes.

Example 2. Identification of an Immunologically Important Hypervariable Domain of the Major Outer Surface Protein A of Borrelia

This Example describes epitope mapping studies using chemically cleaved OspA and TrpE-OspA fusion proteins. The studies indicate a hypervariable region surrounding the single conserved tryptophan residue of OspA (at residue 216, or in some cases 217), as determined by a moving window population analysis of OspA from fifteen European and North American isolates of Borrelia. The hypervariable region is important for immune recognition.

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Site-directed mutagenesis was also conducted to examine the hypervariable regions more closely. Fluorescence and circular dichroism spectroscopy have indicated that the conserved tryptophan is part of an 5 alpha-helical region in which the tryptophan is buried in a hydrophobic environment (McGrath, B.C., et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York; pp. 365-370 (1993)). More polar amino acid side-chains flanking the tryptophan are likely to be exposed to the 10 hydrophilic solvent. The hypervariability of these solvent-exposed residues among the various strains of Borrelia suggested that these amino acid residues may contribute to the antigenic variation in OspA. Therefore, site-directed mutagenesis was performed to replace some of 15 The potentially exposed amino acid side chains in the protein from one strain with the analogous residues of a second strain. The altered proteins were then analyzed by Western Blot using monoclonal antibodies which bind OspA on the surface of the intact, non-mutated spirochete. 20 results indicated that certain specific amino acid changes near the tryptophan can abolish reactivity of OspA to these monoclonal antibodies.

A. Verification of Clustered Polymorphisms in Outer Surface Protein A Sequences

Cloning and sequencing of the OspA protein from fifteen European and North American isolates (described above in Table I) demonstrated that amino acid polymorphism is not randomly distributed throughout the protein; rather, polymorphism tended to be clustered in three regions of OspA. The analysis was carried out by plotting the moving, weighted average polymorphism of a window (a fixed length subsection of the total sequence) as it is slid along the sequence. The window size in this analysis was thirteen amino acids, based upon the determination of the largest

number of significantly deviating points as established by the method of Tajima (<u>J. Mol. Evol. 33</u>: 470-473 (1991)). The average weighted polymorphism was calculated by summing the number of variant alleles for each site. Polymorphism calculations were weighted by the severity of amino acid replacement (Dayhoff, M.O. et al., in: Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure NBRF, Washington, Vol. 5, Suppl. 3: 345 (1978)). The sum was normalized by the window size and plotted. The amino acid sequence 10 position corresponds to a window that encompasses amino acids 1 through 13. Bootstrap resampling was used to generate 95% confidence intervals on the sliding window analysis. Since Borrelia has been shown to be clonal, the bootstrap analysis should give a reliable estimate of the expected variance out of polymorphism calculations. 15 bootstrap was iterated five hundred times at each position, and the mean was calculated from the sum of all positions. The clonal nature of Borrelia ensures that the stochastic variance that results from differing genealogical histories 20 of the sequence positions (as would be expected if recombination were prevalent) will be minimized.

This test verified that the three regions around the observed peaks all have significant excesses of polymorphism. Excesses of polymorphism were observed in the regions including amino acid residues 132-145, residues 163-177, and residues 208-221 (Figure 3). An amino acid alignment between residues 200 and 220 for B31, K48 and the four site-directed mutants is shown in Figure 4. The amino acid 208-221 region includes the region of OspA which has been modeled as an oriented alpha-helix in which the single tryptophan residue at amino acid 216 is buried in a hydrophobic pocket, thereby exposing more polar amino acids to the solvent (Figure 5) (France, L.L., et al., Biochem. Biophys. Acta 1120: 59 (1992)). These potentially solvent-exposed residues showed considerable variability among the

OspAs from various strains and may be an important component of OspA antigenic variation. For the purposes of generating chimeric proteins, the hypervariable domains of interest are <u>Domain A</u>, which includes amino acid residues 120-140 of OspA; <u>Domain B</u>, which includes residues 150-180; and <u>Domain C</u>, which includes residues 200-216 or 217.

- B. Site-Directed Mutagenesis of the Hypervariable Region
 Site-directed mutagenesis was performed to convert
 residues within the 204-219 domain of the recombinant B31

 10 OspA to the analogous residues of a European OspA variant,
 K48. In the region of OspA between residues 204 and 219,
 which includes the helical domain (amino acids 204-217),
 there are seven amino acid differences between OspA-B31 and
 OspA-K48. Three oligonucleotides were generated, each
 containing nucleotide changes which would incorporate K48
 amino acids at their analogous positions in the B31 OspA
 protein. The oligos used to create the site-directed
 mutants were:
- 5'-CTTAATGACTCTGACACTAGTGC-3' (#613, which converts

 threonine at position 204 to serine, and serine at 206 to
 threonine (Thr204-Ser, Thr206-Ser)) (SEQ ID NO. 1);

 5'-GCTACTAAAAAAACCGGGAAATGGAATTCA-3' (#625, which converts
 alanine at 214 to glycine, and alanine at 215 to lysine
 (Ala214-Gly, Ala215-Lys)) (SEQ ID NO. 2); and

 5'-GCAGCTTGGGATTCAAAAACATCCACTTTAACA-3' (#640, which
 converts asparagine at 217 to aspartate, and glycine at
 219 to lysine (Asn217-Asp, Gly219-Lys)) (SEQ ID NO. 3).

 Site-directed mutagenesis was carried out by
 performing mutagenesis with pairs of the above oligos.
- Three site-directed mutants were created, each with two changes: OspA 613 (Thr204-Ser, Thr206-Ser), OspA 625 (Ala214-Gly, Ala215-Lys), and 640 (Asn217-Asp, Gly219-Lys). There were also two proteins with four changes: OspA 613/625 (Thr204-Ser, Thr206-Ser, Ala214-Gly, Ala215-Lys)

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and OspA 613/640 (Thr204-Ser, Thr206-Ser, Asn217-Asp, Gly219-Lys).

Specificity of Antibody Binding to Epitopes of the Non-mutated Hypervariable Region

Monoclonal antibodies that agglutinate spirochetes, including several which are neutralizing in vitro, recognize epitopes that map to the hypervariable region around Trp216 (Barbour, A.G. et al., Infect. and Immun. 41: 759 (1983); Schubach, W.H. et al., Infect. and Immun. 59:

10 1911 (1991)). Western Blot analysis demonstrated that chemical cleavage of OspA from the B31 strain at Trp 216 abolishes reactivity of the protein with the agglutinating Mab 105, a monoclonal raised against B31 spirochetes (data not shown). The reagent, n-chlorosuccinimide (NCS),

15 cleaves OspA at the Trp 216, forming a 23.2kd fragment and a 6.2kd peptide which is not retained on the Imobilon-P membrane after transfer. The uncleaved material binds Mab 105; however, the 23.2kd fragment is unreactive. Similar Western blots with a TrpE-OspA fusion protein containing

the carboxy-terminal portion of the OspA protein demonstrated that the small 6.2kd piece also fails to bind Mab 105 (Schubach, W.H. et al., <u>Infect. and Immun. 59</u>: 1911 (1991)).

Monoclonal antibodies H5332 and H3TS (Barbour, A.G. et al., Infect. and Immun. 41: 759 (1983)) have been shown by immunofluorescence to decorate the surface of fixed spirochetes (Wilske, B. et al., World J. Microbiol. 7: 130 (1991)). These monoclonals also inhibit the growth of the organism in culture. Epitope mapping with fusion proteins has confirmed that the epitopes which bind these Mabs are conformationally determined and reside in the carboxy half of the protein. Mab H5332 is cross-reactive among all of the known phylogenetic groups, whereas Mab H3TS and Mab 105 seem to be specific to the B31 strain to which they were

raised. Like Mab 105, the reactivities of H5332 and H3TS to OspA are abrogated by fragmentation of the protein at Trp216 (data not shown). Mab 336 was raised to whole spirochetes of the strain P/Gau. It cross-reacts to OspA from group 1 (the group to which B31 belongs) but not to group 2 (of which K48 is a member). Previous studies using fusion proteins and chemical cleavage have indicated that this antibody recognizes a domain of OspA in the region between residues 217 and 273 (data not shown). All of these Mabs will agglutinate the B31 spirochete.

Western Blot Analysis of Antibody Binding to Mutated Hypervariable Regions

Mabs were used for Western Blot analysis of the sitedirected OspA mutants induced in E.coli using the T7 15 expression system (Dunn, J.J. et al., Protein Expression and Purification 1: 159 (1990)). E. coli cells carrying Pet9c plasmids having a site-directed OspA mutant insert were induced at mid-log phase growth with IPTG for four hours at 37°C. Cell lysates were made by boiling an aliquot of the induced cultures in SDS gell loading dye, and this material was then loaded onto a 12% SDS gell (BioRad mini-Protean II), and electrophoresed. proteins were then transferred to Imobilon-P membranes (Millipore) 70V, 2 hour at 4°C using the BioRad mini 25 transfer system. Western analysis was carried out as described by Schubach et al. (Infect. Immun. 59: 1911 (1991)).

Western Blot analysis indicated that only the 625 mutant (Ala214-Gly and Ala215-Lys) retained binding to the agglutinating monoclonal H3TS (data not shown). However, the 613/625 mutant which has additional alterations to the amino terminus of Trp216 (Ser204-Thr and Thr206-Ser) did not bind this monoclonal. Both 640 and 613/640 OspAs which have the Asn217-Asp and Gly219-Lys changes on the carboxy-

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terminal side of Trp216 also failed to bind Mab H3TS. This indicated that the epitope of the B31 OspA which binds H3TS is comprised of amino acid side-chains on both sides of Trp216.

The 613/625 mutant failed to bind Mabs 105 and H5332, while the other mutants retained their ability to bind these Mabs. This is important in light of the data using fusion proteins that indicate that Mab 105 behaves more like Mab H3TS in terms of its serotype specificity and binding to OspA (Wilske, B. et al., Med. Microbiol.

Immunol. 181: 191 (1992)). The 613/625 protein has, in addition to the differences at residues Thr204 and Ser206, changes immediately amino-terminal to Trp216 (Ala214-Gly and Ala215-Lys). The abrogation of reactivity of Mabs 105 and H5332 to this protein indicated that the epitopes of OspA which bind these monoclonals are comprised of residues on the amino-terminal side of Trp216.

The two proteins carrying the Asn217-Asp and Gly219-Lys replacements on the carboxy-terminal side of Trp216 (OspAs 640 and 613/640) retained binding to Mabs 105 and H5332; however, they failed to react with Mab 336, a monoclonal which has been mapped with TrpE-OspA fusion proteins and by chemical cleavage to a more carboxy-terminal domain. This result may explain why Mab 336 failed to recognize the K48-type of OspA (Group 2).

It is clear that amino acids Ser204 and Thr206 play an important part in the agglutinating epitopes in the region of the B31 OspA flanking Trp216. Replacement of these two residues altered the epitopes of OspA that bind Mabs 105, 30 H3TS and H5332. The ability of the 640 changes alone to abolish reactivity of Mab 336 indicated that Thr204 and Ser206 are not involved in direct interaction with Mab 336.

The results indicated that the epitopes of OspA which are available to Mabs that agglutinate spirochetes are comprised at least in part by amino acids in the immediate

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vicinity of Trp216. Since recent circular dichroism analysis indicated that the structures of B31 and K48 OspA differ very little within this domain, it is unlikely that the changes made by mutation have radically altered the overall structure of the OspA protein (France, L.L. et al., Biochem. Biophys. Acta 1120: 59 (1992); and France et al., Biochem. Biophys Acta, submitted (1993)). This hypothesis is supported by the finding that the recombinant, mutant OspAs exhibit the same high solubility and purification properties as the parent B31 protein (data not shown).

In summary, amino acid side-chains at Ser204 and Thr206 are important for many of the agglutinating epitopes. However, a limited set of conservative changes at these sites were not sufficient to abolish binding of all of the agglutinating Mabs. These results suggested that the agglutinating epitopes of OspA are distinct, yet may have some overlap. The results also supported the hypothesis that the surface-exposed epitope around Trp216 which is thought to be important for immune recognition and neutralization is a conformationally-determined and complex domain of OspA.

EXAMPLE 3. Borrelia Strains and Proteins

Proteins and genes from any strain of Borrelia can be utilized in the current invention. Representative strains are summarized in Table I, above.

A. Genes Encoding Borrelia Proteins

The chimeric peptides of the current invention can comprise peptides derived from any Borrelia proteins.

Representative proteins include OspA, OspB, OspC, OspD,

pl2, p39, p41 (fla), p66, and p93. Nucleic acid sequences encoding several Borrelia proteins are presently available (see Table II, below); alternatively, nucleic acid

sequences encoding Borrelia proteins can be isolated and characterized using methods such as those described below.

Table II. References for Nucleic Acid Sequences for Several Proteins of Various Borrelia Strains

Strai n	p93	OspA	p41 (fla)
K48	X69602 (SID 67)	X62624 (SID 8)	X69610 (SID 49)
PGau	SID 73	X62387 (SID 10)	X69612 (SID 51)
DK29 ·		X63412 (SID 137)	X69608 (SID 53)
PKo	X69803 (SID 77)	X65599 (SID 141)	X69613 (SID 131)
PTrob	X69604 (SID 71)	X65598 (SID 135)	X69614 (SID 55)
Ip3	-	X70365 (SID 140)	-
Ip90	ND	Kryuchechnikov, V.N. et al., <u>J.Microbiol.</u> <u>Epid. Immunobiol.</u> <u>12</u> :41-44 (1988) (SID 138)	- .
25015	X70365 (SID 75)	Fikrig, E.S. et al., <u>J. Immunol. 7</u> :2256- 2260 1992) SID 12)	-
B31	Perng, G.C. et al., <u>Infect.</u> <u>Immun. 59:</u> 2070- 74 (1992); Luft, B.J. et al., <u>Infect.</u> <u>Immun: 60:</u> 4309- 4321 (1992) (SID 65)	Bergstrom, S. et al., Mol. Microbiol. 3:479-486 (1989) (SID 6)	Gassmann, G.S. et al., <u>Nucl.</u> <u>Acids Res. 17</u> : 3590 (1989) (SID 127)
PKal .	-	X69606 (SID 132)	X69611 (SID 129)
ZS7	-	Jonsson, M. et al., <u>Infect. Immun.</u> <u>60</u> :1845-1853 (1992) (SID 134)	_
N40	-	Kryuchechnikov, V.N. et al. (SID 133)	-
PHei	-	X65600 (SID 136)	-
ACAI	-	Kryuchechnikov, V.N. et al. (SID 142)	-
PBo	X69601 (SID 69)	X65605 (SID 139)	X69610 (SID 130)

Numbers with an "X" prefix are GenBank data base accession numbers. SID = SEQ ID NO.

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B. Isolation of Borrelia Genes

Nucleic acid sequences encoding full length, lipidated proteins from known Borrelia strains were isolated using the polymerase chain reaction (PCR) as described below. In addition, nucleic acid sequences were generated which encoded truncated proteins (proteins in which the lipidation signal has been removed, such as by eliminating the nucleic acid sequence encoding the first 18 amino acids, resulting in non-lipidated proteins). proteins were generated which encoded polypeptides of a particular gene (i.e., encoding a segment of the protein which has a different number of amino acids than the protein does in nature). Using similar methods as those described below, primers can be generated from known 15 enucleic acid sequences encoding Borrelia proteins and used to isolate other genes encoding Borrelia proteins. can be designed to amplify all of a gene, as well as to amplify a nucleic acid sequence encoding truncated protein sequences, such as described below for OspC, or nucleic 20 acid sequences encoding a polypeptide derived from a Borrelia protein. Primers can also be designed to incorporate unique restriction enzyme cleavage sites into the amplified nucleic acid sequences. Sequence analysis of the amplified nucleic acid sequences can then be performed 25 using standard techniques.

> Cloning and Sequencing of OspA Genes and Relevant Nucleic Acid Sequences

Borrelia OspA sequences were isolated in the following manner: 100 μl reaction mixtures containing 50 mM KCl, 10 mM TRIS-HCl (pH 8,3), 1.5 mM MgCl₂, 200 μM each NTP, 2.5 units of TaqI DNA polymerase (Amplitaq, Perkin-Elmer/Cetus) and 100 pmol each of the 5' and 3' primers (described below) were used. Amplification was performed in a Perkin-Elmer/Cetus thermal cycler as described (Schubach, W.H. et

al., Infect. Immun. 59:1811-1915 (1991)). The amplicon was visualized on an agarose gel by ethidium bromide staining. Twenty nanograms of the chloroform-extracted PCR product were cloned directly into the PC-TA vector (Invitrogen) by following the manufacturer's instructions. Recombinant colonies containing the amplified fragment were selected, the plasmids were prepared, and the nucleic acid sequence of each OspA was determined by the dideoxy chain-termination technique using the Sequenase kit (United States Biochemical). Directed sequencing was performed with M13 primers followed by OspA-specific primers derived from sequences, previously obtained with M13 primers.

Because the 5' and 3' ends of the OspA gene are highly conserved (Fikrig, E.S. et al., J. Immunol. 7:2256-2260

15 (1992); Bergstrom, S. et al., Mol. Microbiol. 3: 479-486 (1989); Zumstein, G. et al., Med. Microbiol. Immunol. 181: 57-70 (1992)), the 5' and 3' primers for cloning can be based upon any known OspA sequences. For example, the following primers based upon the OspA nucleic acid sequence 20 from strain B31 were used:

5'-GGAGAATATTATGAAA-3' (-12 to +6) (SEQ ID NO. 4); and 5'-CTCCTTATTTTAAAGCG-3' (+826 to +809) (SEQ ID NO. 5). (Schubach, W.H. et al., <u>Infect. Immun 59</u>:1811-1915 (1991)).

OspA genes isolated in this manner include those for strains B31, K48, PGau, and 25015; the nucleic acid sequences are depicted in the sequence listing as SEQ ID NO. 6 (OspA-B31), SEQ ID NO. 8 (OspA-K48), SEQ ID NO. 10 (OspA-PGau), and SEQ ID NO. 12 (OspA-25015). An alignment of these and other OspA nucleic acid sequences is shown in Figure 42. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 7 (OspA-B31), SEQ ID NO. 9 (OspA-K48), SEQ ID NO. 11 (OspA-PGau), and SEQ ID NO. 13 (OspA-25015).

The following primers were used to generate specific nucleic acid sequences of the OspA gene, to be used to

generate chimeric nucleic acid sequences (as described in Example 4):

- 5'-GTCTGCAAAACCATGACAAG-3' (plus strand primer #369) (SEQ ID NO. 14);
- 5 5'-GTCATCAACAGAAGAAAATTC-3' (plus strand primer #357) (SEQ ID NO 15);
 - 5'-CCGGATCCATATGAAAAAATATTTATTGGG-3' (plus strand primer #607) (SEQ ID NO. 16);
- 5'-CCGGGATCCATATGGCTAAGCAAAATGTTAGC-3' (plus strand primer 10 #584) (SEQ ID NO. 17);
 - 5'-GCGTTCAAGTACTCCAGA-3' (minus strand primer #200) (SEQ ID NO. 18);
 - 5'-GATATCTAGATCTTATTTTAAAGCGTT-3' (minus strand primer #586) (SEQ ID NO. 19); and
- 15 5'-GGATCCGGTGACCTTTTAAAGCGTTTTTAAT-3' (minus strand primer #1169) (SEQ ID NO. 20).

Cloning and Sequencing of OspB

Similar methods were also used to isolate OspB genes.
One OspB genes isolated is represented as SEQ ID NO. 21
20 (OspB-B31); its encoded amino acid sequence is SEQ ID NO.
22.

The following primers were used to generate specific nucleic acid sequences of the OspB gene, to be used in generation of chimeric nucleic acid sequences (see Example 25 4):

- 5'-GGTACAATTACAGTACAA-3' (plus strand primer #721) (SEQ ID NO. 23);
- 5'-CCGAGAATCTCATATGGCACAAAAAGGTGCTGAGTCAATTGG-3' (plus strand primer #1105) (SEQ ID NO. 24);
- 30 5'-CCGATATCGGATCCTATTTTAAAGCGTTTTTAAGC-3' (minus strand
 primer # 1106) (SEQ ID NO. 25); and
 5'-GGATCCGGTGACCTTTTAAAGCGTTTTTAAG-3' (minus strand primer
 #1170) (SEQ ID NO. 26).

Cloning and Sequencing of OspC

Similar methods were also used to isolate OspC genes. The following primers were used to isolate entire OspC genes from Borrelia strains B31, K48, PKO, and pTrob:

5'-GTGCGCGACCATATGAAAAAGAATACATTAAGTGCG-3' (plus strand

primer having Ndel site combined with start codon) (SEQ ID NO. 27), and

5'-GTCGGCGGATCCTTAAGGTTTTTTTGGACTTTCTGC-3' (minus strand primer having BamHl site followed by stop codon) (SEQ ID NO. 28).

The nucleic acid sequences of the OspC genes were then determined by the dideoxy chain-termination technique using the Sequenase kit (United States Biochemical). OspC genes isolated and sequenced in this manner include those for strains B31, K48, PKo, and Tro; the nucleic acid sequences are depicted in the sequence listing as SEQ ID NO. 29 (OspC-B31), SEQ ID NO. 31 (OspC-K48), SEQ ID NO. 33 (OspC-PKO), and SEQ ID NO. 35 (OspC-Tro). An alignment of these sequences is shown in Figure 38. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 30 (OspC-B31), SEQ ID NO. 32 (OspC-K48), SEQ ID NO. 34 (OspC-PKo), and SEQ ID NO. 36 (OspC-Tro).

Truncated OspC genes were generated using other

25 primers. These primers were designed to amplify nucleic
acid sequences, derived from the OspC gene, that lacked the
nucleic acids encoding the signal peptidase sequence of the
full-length protein. The primers corresponded to bp 58-75
of the natural protein, with a codon for Met-Ala attached
30 ahead. For strain B31, the following primer was used:
5'-GTGCGCGACCATATGGCTAATAATTCAGGGAAAGAT-3' (SEQ ID NO.
37).

For strain PKo,

5'-GTGCGCGACCATATGGCTAGTAATTCAGGGAAAGGT-3' (SEQ ID NO. 38)

For strains pTrob and K48, 5'-GTGCGCGACCATATGGCTAATAATTCAGGTGGGGAT-3' (SEQ ID NO. 39) was used.

Additional primers were also designed to amplify nucleic acids encoding particular polypeptides, for use in creation of chimeric nucleic acid sequences (see Example 4). These primers included:

- 5'-CTTGGAAAATTATTTGAA-3' (plus strand primer #520) (SEQ ID NO. 40);
- 5'-CACGGTCACCCCATGGGAAATAATTCAGGGAAAGG-3' (plus strand primer #58) (SEQ ID NO. 41);
 - 5'-TATAGATGACAGCAACGC-3' (minus strand primer #207) (SEQ ID NO. 42); and
- 5'-CCGGTGACCCCATGGTACCAGGTTTTTTTGGACTTTCTGC-3' (minus strand primer #636) (SEQ ID NO. 43).

Cloning and Sequencing of OspD

Similar methods can be used to isolate OspD genes. An alignment of four OspD nucleic acid sequences (from strains pBo, PGau, DK29, and K48) is shown in Figure 39.

20 Cloning and Sequencing of p12

The p12 gene was similarly identified. Primers used to clone the entire p12 gene included: 5'CCGGATCCATATGGTTAAAAAAATAATATTTTTTC-3' (forward primer # 757) (SEQ ID NO. 44); and 5'-

25 GATATCTAGATCTTTAATTGCTCTGCTCACTCTTC-3' (reverse primer #758) (SEQ ID NO. 45).

To amplify a truncated p12 gene (one in which the transcribed protein is non-lipidated, and begins at amino acid 18 of the native sequence), the following primers were used: 5'-CCGGGATCCATATGGCTAGTGCAATTGGTCGTGG-3' (forward primer # 759) (SEQ ID NO. 46); and primer #758 (SEQ ID NO. 45).

Cloning and Sequencing of p41 (fla)

A similar approach was used to clone and sequence genes encoding the p41 (fla) protein. The p41 sequences listed in Table II with GenBank accession numbers were isolated using the following primers from strain B31: 5'-ATGATTATCAATCATAAT-3' (+1 to +18) (SEQ ID NO. 47); and 5'-TCTGAACAATGACAAAAC-3' (+1008 to +991) (SEQ ID NO. 48). The nucleic acid sequences of p41 isolated in this manner are depicted in the sequence listing as SEQ ID NO. 51 (p41-PGau), and SEQ ID NO. 53 (p41-DK29). An alignment of 10 several p41 nucleic acid sequences, including those for strains B31, pKa1, PGau, pBo, DK29, and pKo, is shown in Figure 41. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as 15 SEQ ID NO. 50 (p41-K48), SEQ ID NO. 52 (p41-PGau), SEQ ID NO. 54 (p41-DK29), SEQ ID NO. 56 (p41-PTrob), and SEQ ID NO. 58 (p41-PHei).

Other primers were designed to amplify nucleic acid sequences encoding polypeptides of p41, to be used in chimeric nucleic acid sequences. These primers included: 5'-TTGGATCCGGTCACCCCATGGCTCAATATAACCAATG-3' (minus strand primer #122) (SEQ ID NO. 59);

- 5'-TTGGATCCGGTCACCCCATGGCTTCTCAAAATGTAAG-3' (plus strand primer # 140) (SEQ ID NO. 60);
- 5'-TTGGATCCGGTGACCAACTCCGCCTTGAGAAGG-3' (minus strand primer # 234) (SEQ ID NO. 61); and
 - 5'-TTGGATCCGGTGACCTATTTGAGCATAAGATGC-3' (minus strand primer #141) (SEQ ID NO. 62).

Cloning and Sequencing of p93

The same approach was also used to clone and sequence p93 protein. Genes encoding p93, as listed in Table II with GenBank accession numbers, were isolated by this method with the following primers from strain B31:

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- 5'-GGTGAATTTAGTTGGTAAGG-3' (-54 to -35) (SEQ ID NO. 63); and
- 5'-CACCAGTTTCTTTAAGCTGCTCCTGC-3' (+1117 to +1092) (SEQ ID NO. 64).
- The nucleic acid sequences of p93 isolated in this manner are depicted in the sequence listing as SEQ ID NO. 65 (p93-B31), SEQ ID NO. 67 (p93-K48) SEQ ID NO. 69 (p93-PBo), SEQ ID NO. 71 (p93-PTrob), SEQ ID NO. 73 (p93-PGau), SEQ ID NO. 75 (p93-25015), and SEQ ID NO. 77 (p93-PKo).
- The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 66 (p93-B31), SEQ ID NO. 68 (p93-K48) SEQ ID NO. 70 (p93-PBo), SEQ ID NO. 72 (p93-PTrob), SEQ ID NO. 74 (p93-PGau), SEQ ID NO. 76 (p93-25015), and SEQ ID NO. 78 (p93-PKo).
- Other primers were used to amplify nucleic acid sequences encoding polypeptides of p93 to be used in generating chimeric nucleic acid sequences. These primers included:
- 5'-CCGGTCACCCCATGGCTGCTTTAAAGTCTTTA-3' (plus strand primer 20 #475) (SEQ ID NO. 79);
 - 5'-CCGGTCACCCCATGAATCTTGATAAAGCTCAG-3' (plus strand primer #900) (SEQ ID NO. 80);
 - 5'-CCGGTCACCCCATGGATGAAAAGCTTTTAAAAAGT-3' (plus strand primer #1168) (SEQ ID NO. 81);
- 5'-CCGGTCACCCCCATGGTTGAGAAATTAGATAAG-3' (plus strand primer #1423) (SEQ ID NO. 82); and
 - 5'-TTGGATCCGGTGACCCTTAACTTTTTTAAAG-3' (minus strand primer # 2100) (SEQ ID NO. 83).

C. Expression of Proteins from Borrelia Genes

The nucleic acid sequences described above can be incorporated into expression plasmids, using standard techniques, and transfected into compatible host cells in order to express the proteins encoded by the nucleic acid

sequences. As an example, the expression the p12 gene and the isolation of p12 protein is set forth.

Amplification of the pl2 nucleic acid sequence was conducted with primers that included a NdeI restriction site into the nucleic acid sequence. The PCR product was extracted with phenol/chloroform and precipitated with The precipitated product was digested and ligated into an expression plasmid as follows: 15 μ l (approximately 1 μ g) of PCR DNA was combined with 2 μ l 10X. restriction buffer for NdeI (Gibco/BRL), 1 μ l NdeI 10 (Gibco/BRL), and 2 μ l distilled water, and incubated overnight at 37°C. This mixture was subsequently combined with 3 μ l 10% buffer (buffer 3, New England BioLabs), 1 μ l BamHI (NEB), and 6 μ l distilled water, and incubated at 37° for two hours. The resultant material was purified by 15 preparative gel electrophoresis using low melting point agarose, and the band was visualized under long wave ultraviolet light and excised from the gel. The gel slice was treated with Gelase using conditions recommended by the manufacturer (Epicentre Technologies). The resulting DNA 20 pelled was resuspended in 25-50 μl of 10 mM TRIS-CL (pH 8.0) and 1 mM EDTA (TE). An aliquot of this material was ligated into the Pet9c expression vector (Dunn, J. J. et al., Protein Expression and Purification 1: 159 (1990)).

To ligate the material into the Pet9c expression vector, 20-50 ng of p12 nucleic acid sequences cut and purified as described above was combined with 5 μ l 10 One-Phor-All (OPA) buffer (Pharmacia), 30-60 ng Pet9c cut with NdeI and BamHI, 2.5 μ l 20 mM ATP, 2 μ l T4 DNA ligase (Pharmacia) diluted 1:5 in 1% OPA buffer, and sufficient distilled water to bring the final volume to 50 μ l. The mixture was incubated at 12°C overnight.

The resultant ligations were transformed into competent DH5-alpha cells and plated on nutrient agar plates containing 50 $\mu g/ml$ kanamycin and incubated

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overnight at 37 °C. DH5-alpha is used as a "storage strain" for T7 expression clones, because it is RecA deficient, so that recombination and concatenation are not problematic, and because it lacks the T7 RNA polymerase gene necessary to express the cloned gene. The use of this strain allows for cloning of potentially toxic gene products while minimizing the chance of deletion and/or rearrangement of the desired genes. Other cell lines having similar properties may also be used.

Kanamycin resistant colonies were single-colony purified on nutrient agar plates supplemented with kanamycin at 50 μ g/ml. A colony from each isolate was inoculated into 3-5 ml of liquid medium containing 50 μ g/ml kanamycin, and incubated at 37°C without agitation.

15 Plasmid DNA was obtained from 1 ml of each isolate using a hot alkaline lysis procedure (Mantiatis, T. et al., Molecular Cloning: A Laboratory Manual, cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1982)).

Plasmid DNA was digested with EcoRI and BglII in the following manner: 15 μ l plasmid DNA was combined with 2 μ l 10% buffer 3 (NEB), 1 μ EcoRI (NEB), 1 μ l BglII (NEB) and 1 μ l distilled water, and incubated for two hours at 37°C. The entire reaction mixture was electrophoresed on an analytical agarose gel. Plasmids carrying the p12 insert were identified by the presence of a band corresponding to

925 base-pairs (full length pl2) or 875 base-pairs (nonlipidated pl2).

One or two plasmid DNAs from the full length and nonlipidated p12 clones in Pet9c were used to transform BL21 DE3 pLysS to kanamycin resistance as described by Studier et al. (Methods in Enzymology, Goeddel, D. (Ed.), Academic Press, 185: 60-89 (1990)). One or two transformants of the full length and nonlipidated clones were single-colony purified on nutrient plates containing 25 μ g/ml chloramphenicol (to maintain pLysS) and 50 μ g/ml

kanamycin at 37 °C. One colony of each isolate was inoculated into liquid medium supplemented with chloramphenicol and kanamycin and incubated overnight at The overnight culture was subcultured the following morning into 500 ml of liquid broth with chloramphenicol (25 μ g/ml) and kanamycin (50 μ g/ml) and grown with aeration at 37°C in an orbital air-shaker until the absorbance at 600 nm reached 0.4-0.7. Isopropyl-thio-galactoside (IPTG) was added to a final concentration of 0.5 mM, for induction, and the culture was incubated for 3-4 hours at 10 37° as before. The induced cells were pelleted by centrifugation and resuspended in 25 ml of 20 mM NaPO, (pH 7.7). A small aliquot was removed for analysis by gel electrophoresis. Expressing clones produced proteins which migrated at the 12 kDa position. 15

A crude cell lysate was prepared from the culture as described for recombinant OspA by Dunn, J.J. et al., (Protein Expression and Purification 1: 159 (1990)). crude lysate was first passed over a Q-sepharose column 20 (Pharmacia) which had been pre-equilibrated in Buffer A: 10 mM NaPO4 (pH 7.7), 10 mM NaCl, 0.5 mM PMSF. The column was washed with 10 mM NaPO4, 50 mM NaCl and 0.5 mM PMSF and then pl2 was eluted in 10 mM NaPO4, 0.5 mM PMSF with a NaCl gradient from 50-400 mM. pl2 eluted approximately halfway through the gradient between 100 and 200 mM NaCl. The peak 25 fractions were pooled and dialyzed against 10 mM NaPo4 (pH 7.7), 10 mM NaCl, 0.5 mM PMSF. The protein was then concentrated and applied to a Sephadex G50 gel filtration column of approximately 50 ml bed volume (Pharmacia), in 10 mM NaPO4, 200 mM NaCl, 0.5 mM PMSF. p12 would typically elute shortly after the excluded volume marker. Peak fractions were determined by running small aliquots of all fractions on a gel. The p12 peak was pooled and stored in small aliquots at -20°C.

Example 4. Generation of Chimeric Nucleic Acid Sequences and Chimeric Proteins

A. General Protocol for Creation of Chimeric Nucleic Acid Sequences

The megaprimer method of site directed mutagenesis and its modification were used to generate chimeric nucleic acid sequences (Sarkar and Sommer, <u>Biotechniques 8(4):</u> 404-407 (1990); Aiyar, A. and J. Leis, <u>Biotechniques 14(3):</u> 366-369 (1993)). A 5' primer for the first genomic

template and a 3' fusion oligo are used to amplify the desired region. the fusion primer consists of a 3' end of the first template (DNA that encodes the amino-proximal polypeptide of the fusion protein), coupled to a 5' end of the second template (DNA that encodes the carboxy-proximal polypeptide of the fusion protein).

The PCR amplifications are performed using Taq DNA polymerase, 10X PCR buffer, and ${\rm MgCl_2}$ (Promega Corp., Madison, WI), and Ultrapure dNTPs (Pharmacia, Piscataway, NJ). One $\mu{\rm g}$ of genomic template 1, 5 μ of 10 $\mu{\rm M}$ 5' oligo and 5 $\mu{\rm l}$ of 10 $\mu{\rm M}$ fusion oligo are combined with the following reagents at indicated final concentrations: 10X Buffer-Mg FREE (1X), MgCl₂ (2 mM), dNTP mix (200 $\mu{\rm M}$ each dNTP), Taq DNA polymerase (2.5 units), water to bring final

Norwalk, CT) is used to amplify under the following conditions: 35 cycles at 95°C for one minute, 55°C for two minutes, and 72° for three minutes. This procedure results in a "megaprimer".

volume to 100 μ l. A Thermal Cycler (Perkin Elmer Cetus,

The resulting megaprimer is run on a 1% TAE, 4% low- 30 melt agarose gel. The megaprimer band is cut from the gel and purified using the Promega Magic PCR Preps DNA purification system. Purified megaprimer is then used in a second PCR step. One μg of genomic template 2, approximately 0.5 μg of the megaprimer, and 5 μ of 10 μM 3'

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oligo are added to a cocktail of 10X buffer, MgCl2, dNTPs and Tag at the same final concentrations as noted above, and brought to 100 μ l with water. PCR conditions are the same as above. The fusion product resulting from this 5 amplification is also purified using the Promega Magic PCR Preps DNA purification system.

The fusion product is then ligated into TA vector and transformed into E. coli using the Invitrogen (San Diego, CA) TA Cloning Kit. Approximately 50 ng of PCR fusion product is ligated to 50 ng of pCRII vector with 1X Ligation Buffer, 4 units of T4 ligase, and brought to 10 Nl with water. This ligated product mixture is incubated at 12°C overnight (approximately 14 hours). Two μ l of the ligation product mixture is added to 50 μ l competent INC F' cells and 2 μ beta mercaptoethanol. The cells are then incubated for 30 minutes, followed by heat shock treatment at 42°C for 60 seconds, and an ice quenching for two minutes. 450 μ l of warmed SOC media is then added to the cells, resulting in a transformed cell culture which is incubated at 37°C for one hour with slight shaking. of the transformed cell culture is plated on LB + 50 $\mu g/\tilde{\mu}l$ ampicillin plates and incubated overnight at 37°C. white colonies are picked and added to individual overnight cultures containing 3 ml LB with ampicillin (50 $\mu \mathrm{g}/\mu \mathrm{l}$).

The individual overnight cultures are prepared using Promega's Magic Miniprep DNA purification system. A small amount of the resulting DNA is cut using a restriction digest as a check. DNA sequencing is then performed to check the sequence of the fusion nucleic acid sequence, 30 using the United States Biochemical (Cleveland, OH) Sequenase Version 2.0 DNA sequencing kit. Three to five μg of plasmid DNA is used per reaction. 2 μ l 2M NaOH/2mM EDTA are added to the DNA, and the volume is brought to 20 μ l with water. The mixture is then incubated at room temperature for five minutes. 7 μ l water, 3 μ l 3M NaÅc, 75

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μl EtOH are added. The resultant mixture is mixed by vortex and incubated for ten minutes at -70°C, and then subjected to microfugation. After microfuge for ten minutes, the supernatant is aspirated off, and the pellet is dried in the speed vac for 30 second. 6 μl water, 2 μl annealing buffer, and 2 μl of 10 μM of the appropriate oligo is then added. This mixture is incubated for 10 minutes at 37°C and then allowed to stand at room temperature for 10 minutes. Subsequently, 5.5 μl of label cocktail (described above) is added to each sample of the mixture, which are incubated at room temperature for an additional five minutes. 3.5 μl labeled DNA is then added to each sample which is then incubated for five minutes at 37°C. 4 μl stop solution is added to each well. The DNA is denatured at 95° for two minutes, and then placed on ice.

Clones with the desired fusion nucleic acid sequences are then recloned in frame in the pEt expression system in the lipidated (full length) and non-lipidated (truncated, i.e., without first 17 amino acids) forms. The product is amplified using restriction sites contained in the PCR primers. The vector and product are cut with the same enzymes and ligated together with T4 ligase. The resultant plasmid is transformed into competent E. coli using standard transformation techniques. Colonies are screened as described earlier and positive clones are transformed into expression cells, such as E. coli BL21, for protein expression with IPTG for induction. The expressed protein in its bacterial culture lysate form and/or purified form 30 is then injected in mice for antibody production. The mice are bled, and the sera collected for agglutination, in vitro growth inhibition, and complement- dependent and independent lysis tests.

B. Specific Chimeric Nucleic Acid Sequences

Various chimeric nucleic acid sequences were generated. The nucleic acid sequences are described as encoding polypeptides from Borrelia proteins. The chimeric nucleic acid sequences are produced such that the nucleic acid sequence encoding one polypeptide is in the same reading frame as the nucleic acid sequence encoding the next polypeptide in the chimeric protein sequence encoded by the chimeric nucleic acid sequence. The proteins are listed sequentially (in order of presence of the encoding 10 sequence) in the description of the chimeric nucleic acid sequence. For example, if a chimeric nucleic acid sequence consists of bp 1-650 from OspA-1 and bp 651-820 from OspA-2 were sequenced, the sequence of the chimer would include 15 the first 650 base pairs from OspA-1 followed immediately by base pairs 651-820 of OspA-2.

OspA-K48/OspA-PGau A chimer of OspA from strain K48 (OspA-K48) and OspA from strain PGau (OspA-PGau) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-654 from OspA-K48, followed by bp 655-820 from OspA-PGau. Primers used included: the amino-terminal sequence of OspA primer #607 (SEQ ID NO. 16); the fusion primer,

5'-AAAGTAGAAGTTTTTGAATCCCATTTTCCAGTTTTTT-3' (minus strand primer #668-654) (SEQ ID NO. 84); the carboxy-terminal sequence of OspA primer #586 (SEQ ID NO. 19); and the sequence primers #369 (SEQ ID NO. 14) and #357 (SEQ ID NO. 15). The chimeric nucleic acid sequence is presented as SEQ ID NO. 85; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 86.

OspA-B31/OspA-PGau A chimer of OspA from strain B31 (OspA-B31) and OspA from strain PGau (OspA-PGau) was generated

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using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-PGau. Primers used included: the fusion primer,

5'-AAAGTAGAAGTTTTTGAATTCCAAGCTGCAGTTTT-3' (minus strand primer #668-651) (SEQ ID NO. 87); and the sequence primer, #369 (SEQ ID NO. 14). The chimeric nucleic acid sequence is presented as SEQ ID NO. 88; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 89.

OspA-B31/OspA-K48 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-K48 Primers used included to

bp 652-820 from OspA-K48. Primers used included: the fusion primer,

5'-AAAGTGGAAGTTTTTGAATTCCAAGCTGCAGTTTTTTT-3' (minus strand primer #671-651) (SEQ ID NO. 90); and the sequence primer, #369 (SEQ ID NO. 14). The chimeric nucleic acid sequence

20 is presented as SEQ ID NO. 91; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 92.

OspA-B31/OspA-25015 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain 25015 (OspA-25015) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-25015. Primers used included: the fusion primer, 5'-TAAAGTTGAAGTGCCTGCATTCCAAGCTGCAGTTT-3' (SEQ ID NO. 93). The chimeric nucleic acid sequence is presented as SEQ ID NO. 94; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 95.

OspA-K48/OspA-B31/OspA-K48 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-570 from OspA-B31, followed by bp 570-651 from OspA-B31, followed by bp 650-820 from OspA-K48. Primers used included: the fusion primer, 5'-CCCCAGATTTTGAAATCTTGCTTAAAACAAC-3' (SEQ ID NO.96); and the sequence primer, #357 (SEQ ID NO.15). The chimeric nucleic acid sequence is presented as SEQ ID NO.97; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO.98.

OSDA-B31/OSDA-K48/OSDA-B31/OSDA-K48

A chimer of OSDA from strain E31 (OSDA-B31) and OSDA from strain K48 (OSDA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-420 from OSDA-B31, followed by 420-570 from OSDA-K48, followed by bp 570-650 from OSDA-B31, followed by bp 651-820 from OSDA-K48. Primers used included: the fusion primer, 5'-CAAGTCTGGTTCCAATTTGCTCTTGTTATTAT-3' (minus strand primer #436-420) (SEQ ID NO. 99); and the sequence primer, #357 (SEQ ID NO. 15). The chimeric nucleic acid sequence is presented as SEQ ID NO. 100; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 101.

OspA-B31/OspB-B31 A chimer of OspA and OspB from strain B31 (OspA-B31, OspB-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspB-B31. Primers used included: the fusion primer, 5'-GTTAAAGTGCTAGTACTGTCATTCCAAGCTGCAGTTTTTTT-3' (minus strand primer #740-651) (SEQ ID NO. 102); the carboxy-terminal sequence of OspB primer #1106 (SEQ ID NO. 25); and the sequence primer #357 (SEQ ID NO. 15). The chimeric

nucleic acid sequence is presented as SEQ ID NO. 103; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 104.

OspA-B31/OspB-B31/OspC-B31 A chimer of OspA, OspB and OspC from strain B31 (OspA-B31, OspB-B31, and OspC-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-650 from OspA-B31, followed by bp 652-820 from OspB-B31, followed by bp 74-630 of OspC-B31. Primers used included: the fusion primer, 5'-TGCAGATGTAATCCCATCCGCCATTTTTAAAGCGTTTTT-3' (SEQ ID NO. 105); and the carboxy-terminal sequence of OspC primer (SEQ ID NO. 28). The chimeric nucleic acid sequence is presented as SEQ ID NO. 106; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 107.

OspC-B31/OspA-B31/OspB-B31 A chimer of OspA, OspB and OspC from strain B31 (OspA-B31, OspB-B31, and OspC-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-630 from OspC-B31, followed by bp 52-650 from OspA-B31, followed by bp 650-820 of OspB-B31. Primers used included: the amino-terminal sequence of OspC primer having SEQ ID NO. 27; the fusion primer, 5'-GCTGCTAACATTTTGCTTAGGTTTTTTTGGACTTTC-3' (minus strand primer #69-630) (SEQ ID NO. 108); and the sequence primers #520 (SEQ ID NO. 40) and #200 (SEQ ID NO. 18). The chimeric nucleic acid sequence is presented as SEQ ID NO. 109; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 110.

30 Additional Chimeric Nucleic Acid Sequences

Using the methods described above, other chimeric nucleic acid sequences were produced. These chimeric

nucleic acid sequences, and the proteins encoded, are summarized in Table 3.

Table III Chimeric Nucleic acid Sequences and the Encoded Proteins

Chimers Generated (base pairs)	SEQ ID NO. (nt)	SEQ ID NO. (protein) .
OspA (52-882) / p93 (1168-2100)	111	112
OspB (45-891) / p41 (122-234)	113	114
OspB (45-891) / p41 (122-295)	115	116
OspB (45-891) / p41 (140-234)	117	118
OspB (45-891) / p41 (140-295)	119	120
OspB (45-891) / p41 (122-234) / OspC (58-633)	121	122
OspA-Tro/OspA-Bo	137	138
OspA-PGau/OspA-Bo	139	140
OspA-B31/OspA-PGau/OspA-B31/ OspA-K48	141	142
OspA-PGau/OspA-B31/OspA-K48	143	144

C. Purification of Proteins Generated by Chimeric Nucleic Acid Sequences

The chimeric nucleic acid sequences described above, as well as chimeric nucleic acid sequences produced by the methods described above, are used to produce chimeric proteins encoded by the nucleic acid sequences. Standard methods, such as those described above in Example 3, concerning the expression of proteins from Borrelia genes, can be used to express the proteins in a compatible host organism. The chimeric proteins can then be isolated and purified using standard techniques.

If the chimeric protein is soluble, it can be purified on a Sepharose column. Insoluble proteins can be solubilized in guanidine and purified on a Ni++ column;

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alternatively, they can be solubilized in 10 mM NaPO₄ with 0.1 - 1% TRIXON X 114, and subsequently purified over an S column (Pharmacia). Lipidated proteins were generally purified by the latter method. Solubility was determined by separating both soluble and insoluble fractions of cell lysate on a 12% PAGE gel, and checking for the localization of the protein by Coomasie staining, or by Western blotting with monoclonal antibodies directed to an antigenic polypeptide of the chimeric protein.

10 Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. such equivalents are intended to be encompassed in the scope of the following claims.

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CLAIMS

What is claimed is:

- 1. A chimeric protein comprising two or more antigenic Borrelia polypeptides, wherein the antigenic Borrelia polypeptides which comprise the chimeric protein do not occur naturally in the same protein in Borrelia.
- 2. The chimeric protein of Claim 1, wherein the antigenic Borrelia polypeptides are from two or more different species of Borrelia.
- The chimeric protein of Claim 2, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
 - 4. The chimeric protein of Claim 3, wherein the antigenic Borrelia polypeptides are from corresponding proteins from two or more different species of Borrelia.
- 5. The chimeric protein of Claim 3, wherein the antigenic
 Borrelia polypeptides are from non-corresponding
 proteins from at least two different species of
 Borrelia.
- 6. The chimeric protein of Claim 1, wherein two or more antigenic *Borrelia* polypeptides are from the same species of *Borrelia*.

- 7. The chimeric protein of Claim 6, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
- 8. The chimeric protein of Claim 7, wherein the antigenic Borrelia polypeptides are from the same protein.
- 9. The chimeric protein of Claim 6, wherein the antigenic Borrelia polypeptides are from different proteins.
- 10. A chimeric protein comprising two antigenic Borrelia polypeptides flanking a tryptophan residue, wherein the amino-proximal polypeptide consists of a polypeptide that is proximal from the single tryptophan residue of a first outer surface protein of Borrelia, and the carboxy-proximal polypeptide consists of a polypeptide that is distal from the single tryptophan residue of a second outer surface protein of Borrelia.
- 20 11. The chimeric protein of Claim 10, wherein the first and second outer surface proteins are from the same species of Borrelia.
- 12. The chimeric protein of Claim 11, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
 - 13. The chimeric protein of Claim 11, wherein the first outer surface protein is outer surface protein B, and

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the second outer surface protein is outer surface protein A.

- 14. The chimeric protein of Claim 10, wherein the first and second outer surface proteins are from different species of *Borrelia*.
- 15. The chimeric protein of Claim 14, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 10 16. The chimeric protein of Claim 14, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
- 17. The chimeric protein of Claim 14, wherein the first

 15 and second outer surface proteins are corresponding proteins selected from the group consisting of: outer surface protein A and outer surface protein B.
- 18. The chimeric protein of Claim 10, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 19. The chimeric protein of Claim 18, wherein the aminoproximal polypeptide further comprises a first,
 second, and third hypervariable domain, the first
 hypervariable domain consisting of residues 120
 through 140 of outer surface protein A, the second
 hypervariable domain consisting of residues 150
 through 180 of outer surface protein A, and the third

hypervariable domain consisting of residues 200 through 217 of outer surface protein A.

- 20. The chimeric protein of Claim 19, wherein the first and second hypervariable domains are derived from outer surface protein A from different species of Borrelia.
- The chimeric protein of Claim 10, further comprising an antigenic Borrelia polypeptide derived from a Borrelia protein selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
- 22. A nucleic acid sequence encoding a chimeric protein comprising two antigenic Borrelia polypeptides,
 wherein the two antigenic Borrelia polypeptides which comprise the chimeric protein do not occur naturally in the same protein in Borrelia.
- 23. The nucleic acid sequence of Claim 22, wherein the antigenic Borrelia polypeptides are from two or more different species of Borrelia.
- 24. The nucleic acid sequence of Claim 23, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
 - 25. The nucleic acid sequence of Claim 24, wherein the antigenic Borrelia polypeptides are from corresponding

proteins from two or more different species of Borrelia.

- 26. The nucleic acid sequence of Claim 24, wherein two or more of the antigenic Borrelia polypeptides are from non-corresponding proteins from different species of Borrelia.
 - 27. The nucleic acid sequence of Claim 22, wherein two or more antigenic *Borrelia* polypeptides are from the same species of *Borrelia*.
- 10 28. The nucleic acid sequence of Claim 27, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
 - 29. The nucleic acid sequence of Claim 28, wherein the antigenic *Borrelia* polypeptides are from the same protein.
- 30. The nucleic acid sequence of Claim 27, wherein the antigenic Borrelia polypeptides are from different proteins.

- 31. A nucleic acid sequence encoding a chimeric protein comprising two antigenic Borrelia polypeptides flanking a tryptophan residue, wherein the aminoproximal polypeptide consists of a polypeptide that is proximal from the single tryptophan residue of a first outer surface protein of Borrelia, and the carboxy-proximal polypeptide consists of a polypeptide that is distal from the single tryptophan residue of a second outer surface protein of Borrelia.
- 10 32. The nucleic acid sequence of Claim 31, wherein the first and second outer surface proteins are from the same species of *Borrelia*.
- 33. The nucleic acid sequence of Claim 32, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 34. The nucleic acid sequence of Claim 32, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
 - 35. The nucleic acid sequence of Claim 31, wherein the first and second outer surface proteins are from different species of *Borrelia*.
- 36. The nucleic acid sequence of Claim 35, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.

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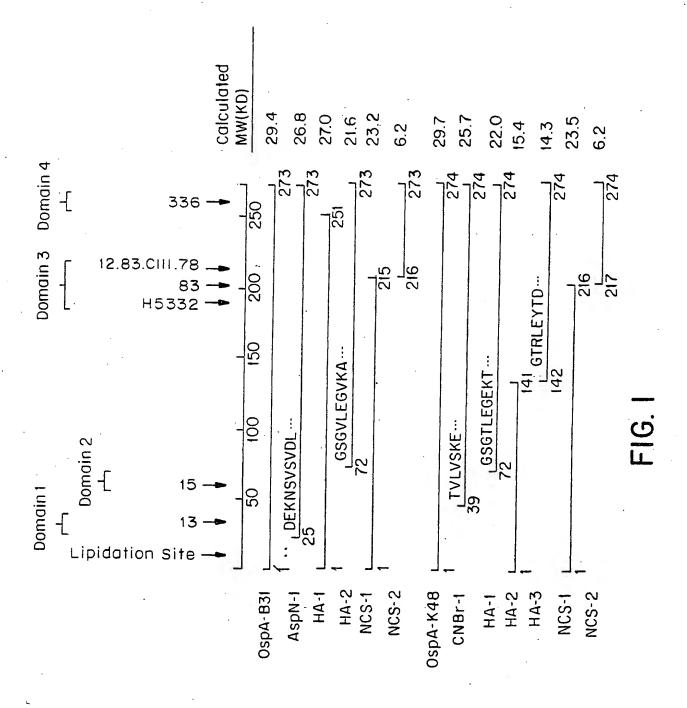
- 37. The nucleic acid sequence of Claim 35, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
- 5 38. The nucleic acid sequence of Claim 35, wherein the first and second outer surface proteins are corresponding proteins selected from the group consisting of: outer surface protein A and outer surface protein B.
- 10 39. The nucleic acid sequence of Claim 31, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 40. The nucleic acid sequence of Claim 39, wherein the
 amino-proximal polypeptide further comprises a first
 and a second hypervariable domain, the first
 hypervariable domain consisting of amino acid residues
 1 through 140 of outer surface protein A, and the
 second hypervariable domain consisting of amino acid
 residues 150 through 217 of outer surface protein A.
 - 41. The nucleic acid sequence of Claim 40, wherein the first and second hypervariable domains are derived from outer surface protein A from different species of Borrelia.
- 25 42. The nucleic acid sequence of Claim 31, further comprising an antigenic Borrelia polypeptide derived from a Borrelia protein selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.

- 43. A nucleic acid sequence having a sequence selected from the group consisting of: SEQ ID NO. 85, SEQ ID NO. 88, SEQ ID NO. 91, SEQ ID NO. 94, SEQ ID NO. 97, SEQ ID NO. 100, SEQ ID NO. 103, SEQ ID NO. 106, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 141, and SEQ ID NO. 143.
- 44. A protein having an amino acid sequence selected from the group consisting of: SEQ ID NO. 86, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 95, SEQ ID NO. 98, SEQ ID NO. 101, SEQ ID NO. 104, SEQ ID NO. 107, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 138, SEQ ID NO. 140, SEQ ID NO. 142, and SEQ ID NO. 144.
- 45. A chimeric protein according to any one of claims 1 to 21 and 44 for use in therapy or diagnosis, for example as a vaccine against <u>Borrelia</u> infection, in immunodiagnostic assays to detect the presence of antibodies to <u>Borrelia</u> or to measure T-cell reactivity.
- 46. A chimeric protein according to claim 45, wherein the immunodiagnostic assay is a dot blot, Western blot, ELISA or agglutination assay.

- 47. Use of the chimeric protein according to any one of claims 1 to 21 and 44, or the nucleic acid sequence of any one of claims 22 to 43, for the manufacture of a compound for use in therapy or diagnosis, for example as a vaccine against <u>Borrelia</u> infection, in immunodiagnostic assays to detect the presence of antibodies to <u>Borrelia</u> or to measure T-cell reactivity.
- 48. Use according to claim 47, wherein the

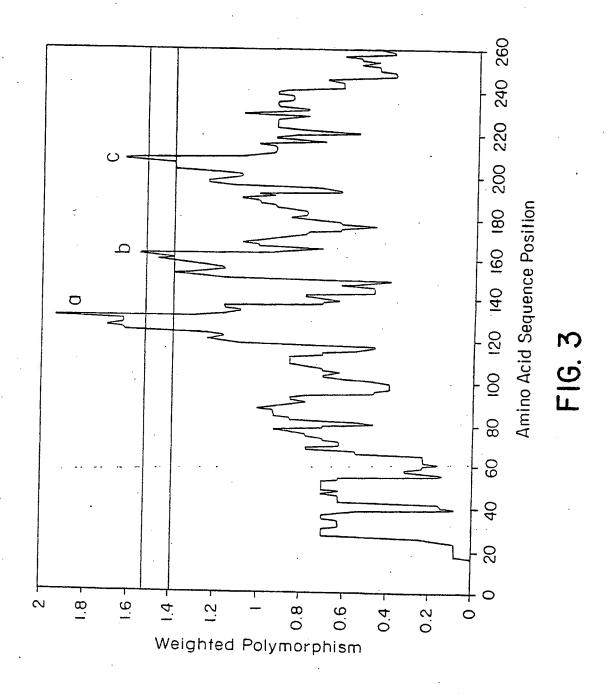
 immunodiagnostic assay is a dot blot, Western blot,

 ELISA or agglutination assay.



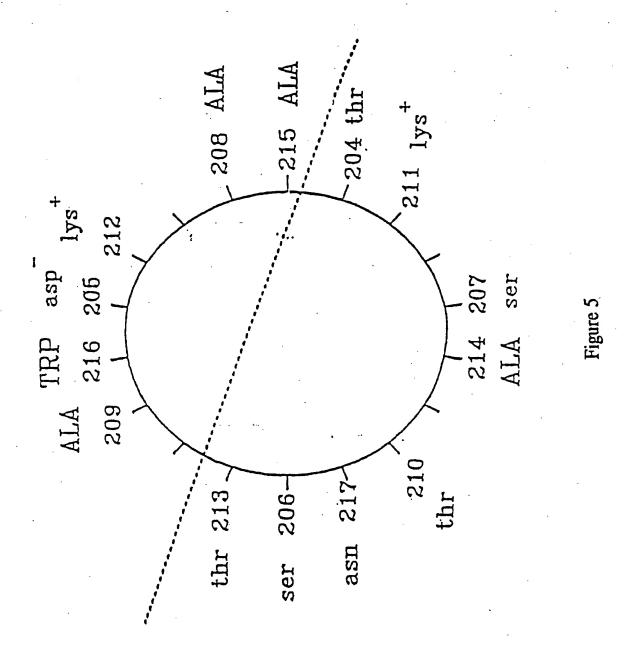
				Domain 1	in 1									Dom	Domain	2				
34 35	5		36	37	38	39	40	41		65	99	67	89	69	70	7.1	72	73	74	75
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190			200		• 4	210		220		250		260		270					•	
IS	KS	GEV	SVELI	NISKSGEVSVELNDTDSSAATKKTAAWNSGT	SSAA	TKKT	JAWN	SGT	A-B31	SNGTKLEGSAVEITKLDEIKN	LEGS	AVEI.	CKLD	EIKN						
15	NS	GEL	TVELI	HIPNSGEITVELNDSNSTQATKKTGKWDSNT	TOA	TKKT	3KWD	SNT	A-TRO	SAGINLEGNAVEIKTLDELKN	LEGN	AVEI	KTLD	ELKN						
Ħ	KS	GEI.	IVAL	NILKSGEITVALDDSDTTQATKKTGKWDSKT	rton.	TKKT	3KWD	SKT	A-K48	SAGTNLEGKAVEITTLKELKN	LEGK	AVEI	LTLK	SLKN						
Ħ	KS	GEL	FAAL	NILKSGEITAALDDSDTTRATKKTGKWDSKT	TRA	FKKTC	KWD	SKT	A-DK29	SAGTNLEGKAVEITTLKELKN	LEGK	AVEI	LTLK	SLKN						
IA	Š	GEV.	TVAL	EIAKSGEVTVALNDTNTTQATKKTGAWDSKT	TTOAT	FKKTC	AMD	SKT	A-P/Gau	SAGTNLEGTAVEIKTLDELKN	LEGT	AVEI	CTLD	SLKN						
IAI	S	GEV	TVAL	EIAKSGEVTVALNDTNTTQATKKTGAWDSKT	TOAT	rkkte	3AWD	SKT	A-PKo	SAGTNLEGTAVEIKTLDELKN	LEGT	AVEI	(TLD	SLKN						
I	Ŝ	GEV	TVAL	EIAKSGEVTVALNDTNTTQATKKTGAWDSKT	TOAT	rkkte	AMD	SKT	A-IP3	SAGTNLEGTAVEIKTLDELKN	LEGT	AVEI	CTLD	ZLKN						
ISN	Š	GEI	TVELA	HISNSGEITVELNDSDTTQATKKTGTWDSKT	TOAT	rkkte	TWD	SKT	A-IP90	SAGINLEGKAVEITTLKELKN	LEGK	AVEI.	TLK	SLKN	٠				,	
ISF	Š	GEV1	TAEL	HISKSGEVTAELNDTDSTQATKKTGKWDAGT	TQA1	PKKTC	KWD.	ηGΤ	A-25015	SAGTNLEGTAVEIKTLDEIKN	EGT	AVEII	(TLD)	SIKN						

igure



K48: ALDDSDTTQATKKTGKWDSKT 613: ELNDSDISAATKKTAAWNSGT 625: ELNDTDSSAATKKTGKWNSGT 640: ELNDTDSSAATKKTAAWQSKT 613/625: ELNDSDISAATKKTGKWNSGT	ELNDIDSSAATKKTAAWNSGT ELND <u>s</u> d <u>s</u> saatkktaawnsgt Elndtdssaatkkt <u>gk</u> wnsgt Elndtdssaatkktaaw <u>d</u> s <u>k</u> t Elnd <u>s</u> d <u>i</u> saatkktgekwnsgt
613/640: ELNDSDISAATKKTAAWDSKT	SKT

Figure



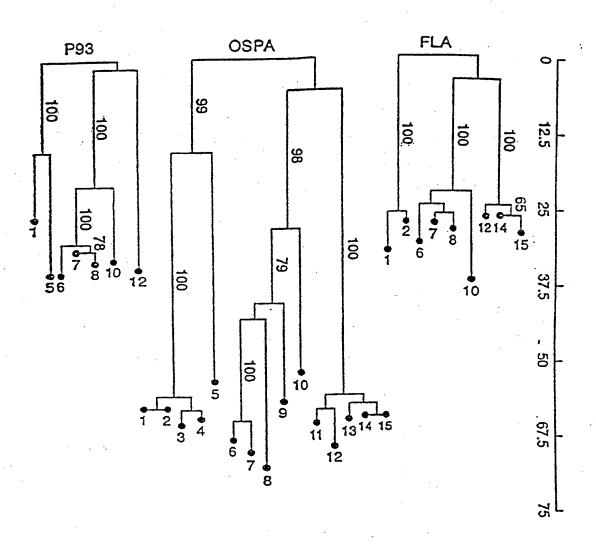


Figure 6

ATC Met	AAI Lys	A AA! E Lys	TAT	TTA Leu 5	TTG Leu	GGA Gly	ATA Ile	GGI Gly	CTA Leu 10	ı Ile	A TTI	A GC	C TT. a Le	A AT	A GCA e Ala 5	4
TGT	Lys Lys	G CAR	AAT Asn 20	ı Val	AGC Ser	AGC Ser	CTI Leu	GAC Asp 25	Glu	AAA Lys	AA A B Asi	AGO A Sez	C GT: Va.	l Se	A GTA r Val	, ,
GAT Asp	TTG	Pro 35	Gly	GAA Glu	ATG Met	AAA Lys	GTT Val 40	Leu	GTA Val	AGC Ser	AAA Lys	GAP Glu 45	Ly	A AAG B ABI	C AAA n Lys	14
GAC Asp	GGC Gly 50	rås	TAC	GAT Asp	CTA Leu	ATT Ile 55	GCA Ala	ACA Thr	GTA Val	GAC Asp	AAG Lys 60	Leu	GAC	CT1	AAA Lys	192
GGA Gly 65	ACT Thr	TCT Ser	GA'T Asp	AAA Lys	AAC Asn 70	AAT	GGA Gly	TCT	GGA Gly	GTA Val 75	Leu	GAA Glu	GC	GTA Val	AAA Lys 80	240
GCT Ala	GAC Asp	AAA Lys	AGT Ser	AAA Lys 85	GTA Val	AAA Lys	TTA Leu	ACA Thr	ATT Ile 90	TCT Ser	GAC	GAT Asp	CTA	GGI Gly 95	CAA Gln	288
ACC Thr	ACA Thr	CTT Leu	GAA Glu 100	GTT Val	TTC Phe	AAA Lys	GAA Glu	GAT Asp 105	GGC Gly	AAA Lys	ACA Thr	CTA Leu	GTA Val 110	Ser	AAA Lys	336
AAA Lys	GTA Val	ACT Thr 115	TCC Ser	AAA Lys	GAC Asp	AAG Lys	TCA Ser 120	TCA Ser	ACA Thr	GAA Glu	GAA Glu	AAA Lys 125	TTC Phe	AAT Asn	GAA Glu	384
AAA Lys	GGT Gly 130	GAA Glu	GTA Val	TCT Ser	GAA Glu	AAA Lys 135	ATA Ile	ATA Ile	ACA Thr	AGA Arg	GCA Ala 140	GAC Asp	GGA Gly	ACC Thr	AGA Arg	432
CTT Leu 145	GAA Glu	TAC Tyr	ACA Thr	GGA Gly	ATT Ile 150	AAA Lys	AGC Ser	GAT Asp.	GGA Gly	TCT Ser 155	Gly	AAA Lys	GCT Ala	AAA Lys	GAG Glu 160	480
GTT /al	TTA Leu	AAA Lys	GTĀ	TAT Tyr 165	GTT Val	CTT Leu	GAA Glu	Gly	ACT Thr 170	CTA Leu	ACT Thr	GCT Ala	GAA Glu	AAA Lys 175	ACA Thr	528
ACA Thr	TTG Leu	GTG Val	GTT Val 180	AAA Lys	GAA Glu	GGA . Gly	Thr	GTT . Val : 185	ACT Thr	TTA Leu	AGC Ser	Lys	AAT Asn 190	ATT Ile	TCA Ser	576
AAA .ys	DEL	GGG Gly 195	GAA Glu	GTT Val	TCA Ser	val (GAA Glu 200	CTT :	AAT Asn	GAC Asp	Thr	GAC Asp 205	AGT Ser	AGT Ser	GCT Ala	624

Figure 7 (1 of 2)

Ala	Thr 210	Lys	Lys	Thr	Ala	Ala 215	Trp	Asn	Ser	GCC	Thr 220	Ser	ACT	Leu	ACA Thr	672
ATT Ile 225	ACT Thr	GTA Val	AAC Asn	AGT Ser	AAA Lys 230	AAA Lys	ACT Thr	AAA Lys	GAC Asp	CTT Leu 235	GTG Val	TTT Phe	ACA Thr	AAA Lys	GAA Glu 240	720
AAC Asn	ACA Thr	ATT	ACA Thr	GTA Val 245	CAA Gln	CAA Gln	TAC Tyr	GAC Asp	TCA Ser 250	AAT Asn	GGC Gly	ACC Thr	AAA Lys	TTA Leu 255	GAG Glu	768
GGG Gly	TCA Ser	GCA Ala	GTT Val 260	GAA Glu	ATT	ACA Thr	AAA Lys	CTT Leu 265	GAT Asp	GAA Glu	ATT Ile	AAA Lys	AAC Asn 270	GCT Ala	TTA Leu	816
AAA	TA															822

Figure 7 (2 of 2)

OSPA K48

ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TTT TTT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala>

50 60 70 80 90

TGT AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAT AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTA TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val>

100 110 120 130 140

GAT TTA CCT GGT GGA ATG ACA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAT GGA CCA CCT TAC TGT CAA GAA CAT TCA TTT CTT TTT CTG TTT Asp Leu Pro Gly Gly Met Thr Val Leu Val Ser Lys Glu Lys Asp Lys>

150 160 170 180 190

GAC GGT AAA TAC AGT CTA GAG GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCA TTT ATG TCA GAT CTC CGT TGT CAT CTG TTC GAA CTC GAA TTT ASP Gly Lys Tyr Ser Leu Glu Ala Thr Val Asp Lys Leu Glu Leu Lys>

200 210 220 230 240

GGA ACT TCT GAT AAA AAC AAC GGT TCT GGA ACA CTT GAA GGT GAA AAA CCT TGA AGA CTA TTT TTG TTG CCA AGA CCT TGT GAA CTT CCA CTT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Thr Leu Glu Gly Glu Lys>

250 260 270 280

ACT GAC AAA AGT AAA GTA AAA TTA ACA ATT GCT GAT GAC CTA AGT CAA TGA CTG TTT TCA TTT CAT TTT AAT TGT TAA CGA CTA CTG GAT TCA GTT Thr Asp Lys Ser Lys Val Lys Leu Thr Ile Ala Asp Asp Leu Ser Gln>

290 300 310 320 330

ACT AAA TTT GAA ATT TTC AAA GAA GAT GCC AAA ACA TTA GTA TCA AAA TGA TTT AAA CTT TAA AAG TTT CTA CGG TTT TGT AAT CAT AGT TTT Thr Lys Phe Glu Ile Phe Lys Glu Asp Ala Lys Thr Leu Val Ser Lys>

340 350 360 370 380

AAA GTA ACC CTT AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAC GAA TTT CAT TGG GAA TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTG CTT Lys Val Thr Leu Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

FIGURE 8 (1 of 3)

OSP A K48

	390			40	0		4	10			420			4:	30
•	•		•		•	•		*			•		•		•
											GCA				
											CGT				
Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
٠															
					450				- ^						
_	4	140			450			46	•		4	170		_	480
~mm	C 3 3	ma C	ארא	CNC	እጥአ	222	AGC.	CAT	CCA	TCC.	GGA	222			C) }
											CCT				
															Glu>
Deu	GIU	*3+		rap		<i>D</i> , <i>D</i>			013		Cly	נעט	774	Lys	GIU>
		49	90		9	500			510			52	20		
	•		•	*		•		•	•		•		•	•	
GTT	TTA	AAA	GAC	TTT	ACT	CTT	GAA	GGA	ACT	CTA	GCT	GCT	GAC	GGC	AAA
											CGA				
Val	Leu	Lys	Asp	Phe	Thr	Leu	Glu	Gly	Thr	Leu	Ala	Ala	Asp	Gly	Lys>
530			540		_	55	50	_	-	60		_	570		
		- mm				C) }	-	·~		~~~	~~·	•	•		•
											ATT TAA				
															Ile>
4111	4 444	שכע	Dy 3	V 41	****	914	013	****	V U1	•	Den	Ser	Lys	ASII	116>
5	во		:	590			600			61	LO			520	
•	•	•		•		•	•		•		*	•		•	
											GAC				
											CTG				
Leu	Lys	Ser	Gly	Glu	Ile	Thr	Val	Ala	Leu	Asp	Asp	Ser	Asp	Thr	Thr>
			•												١.
_	630			6	40		•	550		_	660		_	67	70
CNC		y Call	- 777	***	y Cab -	CCY	* * *	4.C	CAT	ጥሮች	AAA	> Cm	-	٠	-
											TTT				
															Leu>
	, , , , ,		ک رک	<i>ــر</i> د		01,	ی رب		1.00		ay s	* * * * *	Set	1111	neu >
	0	680			690			7	00		•	710			720
•		•		*	•		•		•	•		. •		•	•
ACA	ATT	AGT	GTG	AAT	AGC	CAA	ÄAA	ACC	AAA	AAC	CTT	GTA	TTC	ACA	AAA
															TTT
Thr	Ile	Ser	Val	Asn	Ser	Gln	Lys	Thr	Lys	Asn	Leu	Val	Phe	Thr	Lys>
		٠. 💂	30			740			256						
		7	30			740		•	750		_	7	50	_	
CDN	. C>C	מ יים	- -	ע כע	CTA	C	222	- ጥልቦ	CyC.	ጥርአ	GCA	coc	200		٠٠٠ ع
															CTA GAT
															Leu>
							-23	- 1 -	نود			~ ± y	* ***	UD11	7 C D 2

Osp A K-48

770 780 790 800 810

GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA Glu Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala>

OSP A K48

820

TTA AAA TAA AAT TTT ATT Leu Lys ***>

FIGURE 8 (3 of 3)

OSP A PGAU

		1	.0			20	•		30			4	10		
	•	,	•	◆ ,		•		•	•		*		•	•	•
ATG	AAA	AAA	ŢĄŢ	ATT	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	TTA	ATA	GCA
TAC	TTT	TTT	ATA	TAA	AAC	CCT	TAT	CCA	GAT	TAT	TAA	CGG	AAT	TAT	CGT
Met	Lys	Lys	Tyr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	Ile	Ala>
50			60			7	0			80			90		
•		•	•		•		*	•		•		•	•		•
				GTT											
				CAA											
Cys	Lys	Gln	Asn	Val	Ser	Ser	Leu	Asp	Glu	Lys	Asn	Ser	Ala	Ser	Val>
10	0		1	10	-		120			13	0		3	40	
	*	•		*		•	•		•		•	*		•	
				GAG											
				CTC											
Asp	Leu	Pro	Gly	Glu	Met	Lys	Val	Leu	Val	Ser	Lys	Glu	Lys	Asp	Lys>
	150			16	50		3	70			180	•		19	0
•			•		•	•	_	•		*	•		•		•
GAC	GGT	AAG	TAC	AGT	CTA	AAG	GCA	ACA	GTA	GAC	AAG	ATT	GAG	CTA	AAA
CTG	CCA	TTC	ATG	TCA	GAT	TTC	CGT	TGT	CAT	CTG	TTC	TAA	CTC	GAT	TTT
Asp	Gly	Lys	Tyr	Ser	Leu	Lys	Ala	Thr	Val	Asp	Lys	Ile	Glu	Leu	Lys>
	•	200			210			22	20	•	2	230	**		240
•	•	•		•	•		•		*	•		•		•	•
				AAA											
				TTT											
Gly	Thr	Ser	Asp	Lys	Asp	Asn	CJÀ	Ser	Gly	Val	Leu	Glu	Gly	Thr	Lys>
		2	50		:	260			270			. 2	80		
	•		•	*		*		•	•		•		•	•	
				AAA											
		TTT	TCA	TTT	CGT	TTT	AAT	でして	ጥልል	CGA	CTG	CTA	GAT	TCA	
Asp															7
	Asp	Lys	Ser	Lys									Leu	Ser	Lys
290	Asp	Lys	Ser			Lys			Ile				Leu 330	Ser	Lys
290	Asp	Lys	٠.			Lys	Leu		Ile	Ala				Ser	Lys
ACC	ACA	• TTC	300 • GAA	Lys	Ala TTA	Lys 3 AAA	Leu 10 GAA	Thr GAT	Ile	Ala 320 AAA	ASP	Asp •	330 * GTG	TCA	• AGA
ACC TGG	ACA	TTC	300 GAA CTT	Lys CTT GAA	Ala TTA AAT	Lys 3 AAA TTT	Leu 10 GAA CTT	Thr GAT CTA	Ile GGC CCG	Ala 320 AAA TTT	ASP ACA TGT	Asp TTA AAT	330 GTG CAC	TCA AGT	AGA TCT
ACC TGG	ACA	TTC	300 GAA CTT	Lys CTT GAA	Ala TTA AAT	Lys 3 AAA TTT	Leu 10 GAA CTT	Thr GAT CTA	Ile GGC CCG	Ala 320 AAA TTT	ASP ACA TGT	Asp TTA AAT	330 GTG CAC	TCA AGT	AGA
ACC TGG Thr	ACA	TTC	300 GAA CTT	Lys CTT GAA	Ala TTA AAT	Lys 3 AAA TTT	Leu 10 GAA CTT	Thr GAT CTA Asp	Ile GGC CCG	Ala 320 AAA TTT Lys	ASP ACA TGT	Asp TTA AAT	330 GTG CAC Val	TCA AGT	AGA TCT
ACC TGG Thr	ACA TGT Thr	TTC AAG	300 GAA CTT Glu	CTT GAA Leu 350	Ala TTA AAT Leu	Lys 3 AAA TTT Lys	GAA CTT Glu	GAT CTA Asp	GGC CCG Gly	Ala 320 AAA TTT Lys 3	ASP ACA TGT Thr	ASP TTA AAT Leu	330 GTG CAC Val	TCA AGT Ser 380	AGA TCT Arg>
ACC TGG Thr	ACA TGT Thr	TTC AAG Phe	300 GAA CTT Glu	CTT GAA Leu 350	Ala TTA AAT Leu	AAA TTT Lys	GAA CTT Glu 360	Thr GAT CTA Asp	GGC CCG Gly	Ala 320 AAA TTT Lys 3 GAT	ASP ACA TGT Thr 70 GAA	ASP TTA AAT Leu ATG	330 GTG CAC Val	TCA AGT Ser 380	AGA TCT Arg>
ACC TGG Thr 3	ACA TGT Thr 40 GTA	TTC AAG Phe AGT	300 GAA CTT Glu TCT	CTT GAA Leu 350	Ala TTA AAT Leu GAC	Lys 3 AAA TTT Lys AAA TTT	GAA CTT Glu 360 ACA	GAT CTA Asp	GGC CCG Gly	Ala 320 AAA TTT Lys 3 GAT CTA	ASP ACA TGT Thr 70 GAA CTT	ASP TTA AAT Leu ATG	330 GTG CAC Val	TCA AGT Ser 380	AGA TCT Arg>

FIGURE 9 (1 of 3)

OSP A PGAU

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	300				^^										
	390			4	00		•	410			420			4	30
444	CCT	CAA	TTG	тст	CCA	222	»cc	ATC) C)	Ċ: N	አአጥ	CCN	۸.00	AAA
															TTT
Lvs	Glv	Glu	Leu	Ser	Ala	Lvs	Thr	Met	Thr	Arg	Gli	Acn	GIV	The	Lys
.						-,-				, - 9	010		O.J	2 4 4 4	Lys
		440			450			4	60			470			480
•		•		*	•		•		•	*		•		•	•
CTT	GAA	TAT	ACA	GAA	ATG	AAA	AGC	GAT	GGA	ACC	GGA	AAA	GCT	AAA	GAA
GAA	CII	ATA	TGT	CTT	TAC	TTT	TCG	CTA	CCT	TGG	CCT	TTT	CGA	TTT	CTT
Leu	Glu	Tyr	Thr	Glu	Met	Lys	Ser	Asp	Gly	Thr	Gly	Lys	Ala	Lys	Glu>
		4	90		9	500			510			5:	20		
	•			•		•		*	•		•		•	•	
GTT	TTA	AAA	AAG	TTT	ACT	CTT	GAA	GGA	AAA	GTA	GCT	AAT	GAT	AAA	GTA
CAA	AAT	TTT	TTC	AAA	TGA	GAA	CTT	CCT	TTT	CAT	CGA	TTA	CTA	TTT	CAT
vaı	ren	Lys	Lys	Phe	Thr	Leu	Glu	Gly	Lys	Val	Ala	Asn	Asp	Lys	Val>
530			540		٠.	55	50		9	560			570		
•		•	•		•		•	•		•		•	- •		•
ACA	TTG	GAA	GTA	AAA	GAA	GGA	ACC	GTT	ACT	TTA	AGT	AAG	GAA	ATT	GCA
TGT	AAC	CII	CAT	TTT	CTT	CCT	TGG	CAA	TGA	TAA	TCA	TTC	CTT	TAA	CGT
Thr	Leu	Glu	Val	Lys	Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Glu	Ile	Ala>
5	B0			590			600			61	0			520	
	•	•		•		•	•		•	-	•	•	•		
AAA	TCT	GGA	GAA	GTA	ACA	GTT	GCT	CTT	AAT	GAC	ACT	AAC	ACT	ACT	CAG
TŢŢ	AGA	CCT	CTT	CAT	TGT	CAA	CGA	GAA	TTA	CTG	TGA	TTG	TGA	TGA	GTC
T															
Lys	Ser	Gly	Glu	Val	Thr	Val	Ala	Leu	Asn	Asp	Thr	Asn	Thr	Thr	Gln>
Lys	Ser	Gly	Glu	Val		Val		Leu	Asn	Asp		Asn	Thr		
Lys.	Ser 630	Gly	Glu	Val 64		Val		Leu 50	Asn	Asp	Thr 660	Asn	Thr	Thr 67	
GCT	630 ACT	Gly AAA	Glu • AAA	Val 64 ACT	GGC	• GCA	TGG	Leu 550 • GAT	TCA	AAA	660 *	Asn TCT	Thr • ACT	67 TTA	0 • ACA
GCT CGA	630 ACT TGA	Gly AAA TTT	Glu AAA TTT	Val 64 ACT TGA	GGC CCG	GCA CGT	TGG ACC	Leu 50 GAT CTA	TCA AGT	AAA TTT	660 ACT	ASN TCT AGA	Thr • ACT TGA	67 TTA AAT	0 • ACA TGT
GCT CGA	630 ACT TGA	Gly AAA TTT	Glu AAA TTT	Val 64 ACT TGA	GGC	GCA CGT	TGG ACC	Leu 50 GAT CTA	TCA AGT	AAA TTT	660 ACT	ASN TCT AGA	Thr • ACT TGA	67 TTA AAT	0 • ACA TGT
GCT CGA	630 ACT TGA Thr	AAA TTT Lys	Glu AAA TTT	Val 64 ACT TGA	GGC CCG Gly	GCA CGT	TGG ACC	GAT CTA Asp	TCA AGT Ser	AAA TTT	ACT TGA Thr	ASN TCT AGA Ser	Thr • ACT TGA	67 TTA AAT Leu	0 * ACA TGT Thr>
GCT CGA	630 ACT TGA Thr	Gly AAA TTT	Glu AAA TTT	Val 64 ACT TGA	GGC CCG	GCA CGT	TGG ACC	Leu 50 GAT CTA	TCA AGT Ser	AAA TTT	ACT TGA Thr	ASN TCT AGA	Thr • ACT TGA	67 TTA AAT Leu	0 • ACA TGT
GCT CGA Ala	Ser 630 ACT TGA Thr	AAA TTT Lys	AAA TTT Lys	Val 64 ACT TGA Thr 4 AGC	GGC CCG Gly 690	GCA CGT Ala	TGG ACC Trp	Leu 50 GAT CTA ASP 70	TCA AGT Ser	AAA TTT Lys	660 ACT TGA Thr	TCT AGA Ser 10	Thr ACT TGA Thr	67 TTA AAT Leu	0 ACA TGT Thr>
GCT CGA Ala ATT TAA	630 ACT TGA Thr	AAA TTT Lys 80	AAA TTT Lys AAC TTG	Val 64 ACT TGA Thr AGC TCG	GGC CCG Gly 690	GCA CGT Ala AAA TTT	TGG ACC Trp * ACT TGA	Leu 550 GAT CTA ASP 70 ACA TGT	TCA AGT Ser	AAA TTT Lys CTT GAA	660 ACT TGA Thr 7 GTG CAC	TCT AGA Ser 10	Thr ACT TGA Thr ACT TGA	67 TTA AAT Leu AAA	0 ACA TGT Thr> 720 CAA
GCT CGA Ala ATT TAA	630 ACT TGA Thr	AAA TTT Lys 80	AAA TTT Lys AAC TTG	Val 64 ACT TGA Thr AGC TCG	GGC CCG Gly 690	GCA CGT Ala AAA TTT	TGG ACC Trp * ACT TGA	Leu 550 GAT CTA ASP 70 ACA TGT	TCA AGT Ser	AAA TTT Lys CTT GAA	660 ACT TGA Thr 7 GTG CAC	TCT AGA Ser 10	Thr ACT TGA Thr ACT TGA	67 TTA AAT Leu AAA	0 ACA TGT Thr>
GCT CGA Ala ATT TAA	630 ACT TGA Thr	AAA TTT Lys 80 GTT CAA Val	AAA TTT Lys AAC TTG Asn	Val 64 ACT TGA Thr AGC TCG	GGC CCG Gly 690 AAA TTT Lys	GCA CGT Ala AAA TTT Lys	TGG ACC Trp * ACT TGA	Leu 550 GAT CTA ASP 70 ACA TGT	TCA AGT Ser 00 * CAA GTT Gln	AAA TTT Lys CTT GAA	660 ACT TGA Thr 7 GTG CAC	TCT AGA Ser 10 .* TTT AAA Phe	ACT TGA Thr ACT TGA Thr	67 TTA AAT Leu AAA	0 ACA TGT Thr> 720 CAA
GCT CGA Ala ATT TAA	630 ACT TGA Thr	AAA TTT Lys 80	AAA TTT Lys AAC TTG Asn	Val 64 ACT TGA Thr AGC TCG	GGC CCG Gly 690 AAA TTT Lys	GCA CGT Ala AAA TTT	TGG ACC Trp * ACT TGA	Leu 550 GAT CTA ASP 70 ACA TGT	TCA AGT Ser	AAA TTT Lys CTT GAA	660 ACT TGA Thr 7 GTG CAC	TCT AGA Ser 10	ACT TGA Thr ACT TGA Thr	67 TTA AAT Leu AAA	0 ACA TGT Thr> 720 CAA
GCT CGA Ala ATT TAA Ile	Ser 630 ACT TGA Thr AGT TCA Ser	AAA TTT Lys 80 GTT CAA Val	AAA TTT Lys AAC TTG Asn	ACT TGA Thr AGC TCG Ser	GGC CCG Gly 690 AAA TTT Lys	GCA CGT Ala AAA TTT Lys	TGG ACC Trp * ACT TGA Thr	GAT CTA ASP 70 ACA TGT Thr	TCA AGT Ser O * CAA GTT Gln	AAA TTT Lys CTT GAA Leu	ACT TGA Thr 7 GTG CAC Val	TCT AGA Ser 10 • TTT AAA Phe	ACT TGA Thr ACT TGA Thr	67 TTA AAT Leu AAA TTT Lys	0 ACA TGT Thr> 720 CAA GTT Gln>
GCT CGA Ala ATT TAA Ile	Ser 630 ACT TGA Thr AGT TCA Ser	AAA TTT Lys 80 GTT CAA Val	AAA TTT Lys AAC TTG ASD	ACT TGA Thr AGC TCG Ser	GGC CCG Gly 690 AAA TTT Lys	GCA CGT Ala AAA TTT Lys	TGG ACC Trp ACT TGA Thr	GAT CTA ASP 70 ACA TGT Thr	TCA AGT Ser O CAA GTT Gln 750	AAA TTT Lys CTT GAA Leu	ACT TGA Thr 7 GTG CAC Val	TCT AGA Ser 10 TTT AAA Phe 76	ACT TGA Thr ACT TGA Thr	TTA AAT Leu AAA TTT Lys	0 ACA TGT Thr> 720 CAA GTT Gln>
GCT CGA Ala ATT TAA Ile	Ser 630 ACT TGA Thr AGT TCA Ser ACA TGT	AAA TTT Lys 80 GTT CAA Val 73 ATA TAT	AAA TTT Lys AAC TTG ASD	Val 64 ACT TGA Thr AGC TCG Ser GTA CAT	GGC CCG Gly 690 AAA TTT Lys	GCA CGT Ala AAA TTT Lys 40 CAA GTT	TGG ACC Trp ACT TGA Thr	GAT CTA ASP 70 ACA TGT Thr GAC CTG	TCA AGT Ser O * CAA GTT Gln 750 * TCC AGG	AAA TTT Lys CTT GAA Leu GCA CGT	660 ACT TGA Thr GTG CAC Val	TCT AGA Ser 10 TTT AAA Phe 76 ACC	ACT TGA Thr ACT TGA Thr	TTA AAT Leu AAA TTT Lys TTA AAT	0 ACA TGT Thr> 720 CAA GTT Gln>

FIGURE 9 (2 of 3)

OSP A PGAU

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA
CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT
Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

820
AAA TAA
TTT ATT
Lys ***>

FIGURE 9 (3 of 3)

ATG Met 1	AAA Lys	AAA Lys	TAT Tyr	TTA Leu 5	TTG Leu	GGA Gly	ATA Ile	GGT Gly	CTA Leu 10	ATA Ile	TTA Leu	GCT Ala	TTA Leu	ATA Ile 15	GCA Ala	41	8
TGT Cys	AAG Lys	CAA Gln	AAT Asn 20	GTT Val	AGC Ser	AGC Ser	CTT Leu	GAC Asp 25	GAG Glu	AAA Lys	AAC Asn	AGC Ser	GTT Val 30	TCA Ser	GTA Val	9(5
GAT Asp	TTG Leu	CCT Pro 35	GGT Gly	GAA Glu	ATG Met	AAA Lys	GTT Val 40	CTT Leu	GTA Val	AGC Ser	AAA Lys	GAA Glu 45	AAA Lys	GAC Asp	AAA Lys	144	1
GAC Asp	GGC Gly 50	AAG Lys	TAC Tyr	AGT Ser	CTA Leu	ATG Met 55	GCA Ala	ACA Thr	GTA Val	GAC Asp	AAG Lys 60	CTT Leu	GAG Glu	CTT Leu	AAA Lys	192	2

Figure 10 (1 of 2)

	GGA Gly 65	ACA Thr	TCT Ser	GAT	AAA Lys	AAC Asn 70	AAT Asn	GGA Gly	TCT	GCG	GTG Val 75	CTT Leu	GAA Glu	GGC	GTA Val	AAA Lys 80		240	
	GCT Ala	GAC	AAA Lys	AGC Ser	AAA Lys 85	GTA Val	AAA Lys	TTA Leu	ACA Thr	GTT Val 90	TCT Ser	GAC Asp	GAT Asp	CTA Leu	AGC Ser 95	ACA Thr		288	
	ACC Thr	ACA Thr	CTT	GAA Glu 100	GTT Val	TTA Leu	AAA Lys	GAA Glu	GAT Asp 105	GJÅ GGC	AAA Lys	ACA Thr	TTA Leu	GTG Val 110	TCA Ser	AAA Lys		336	
	AAA Lys	AGA Arg	ACT Thr 115	TCT Ser	AAA Lys	GAT Asp	AAG Lys	TCA Ser 120	TCA Ser	ACA Thr	GAA Glu	GAA Glu	AAG Lys 125	TTC Phe	AAT Asn	GAA Glu		384	
	AAA Lys	GGC Gly 130	GAA Glu	TTA Leu	GTT Val	GAA Glu	AAA Lys 135	ATA Ile	ATG Met	GCA Ala	AGA Arg	GCA Ala 140	AAC Asn	GGA Gly	ACC Thr	ATA Ile	÷	432	
	CTT Leu 145	GAA Glu	TAC Tyr	ACA Thr	GGA Gly	ATT Ile. 150	AAA Lys	AGC Ser	GAT Asp	GGA Gly	TCC Ser 155	GGA Gly	AAA Lys	GCT Ala	AAA Lys	GAA Glu 160		480	
	ACT Thr	TTA Leu	AAA Lys	GAA Glu	TAT Tyr 165	GTT Val	CTT Leu	GAA Glu	GGA Gly	ACT Thr 170	CTA Leu	ACT	GCT Ala	GAA Glu	AAA Lys 175	GCA Ala		528	
	ACA Thr	TTG Leu	GTG Val	GTT Val 180	AAA Lys	GAA Glu	GGA Gly	ACT Thr	GTT Val 185	ACT Thr	TTA Leu	AGT Ser	AAG Lys	CAC His 190	ATT	TCA Ser		576	
		TCT Ser																624	
,	GCT Ala	ACT Thr 210	AAA Lys	AAA Lys	ACT	GGG	AAA Lys 215	TGG Trp	GAT Asp	GCA Ala	GGC Gly	ACT Thr 220	TCA Ser	ACT Thr	TTA Leu	ACA Thr		672	
		ACT Thr																720	
		ACA Thr																768	
		ACA Thr																816	
	AGA Arg															•	٠	819	

Figure 10 (2 of 2)

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OSP B B-31 Sequence Range: 1 to 891

30 20 10 ATG AGA TTA TTA ATA GGA TTT GCT TTA GCG TTA GCT TTA ATA GGA TGT TAC TOT AAT AAT TAT COT AAA CGA AAT CGC AAT CGA AAT TAT COT ACA Met Arg Leu Leu Ile Gly Phe Ala Leu Ala Leu Ile Gly Cys> 90 70 50 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT Ala Gln Lys Gly Ala Glu Ser Ile Gly Ser Gln Lys Glu Asn Asp Leu> 120 130 110 . 100 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG Asn Leu Glu Asp Ser Ser Lys Lys Ser His Gln Asn Ala Lys Gln Asp> 150 160 170 150 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT Leu Pro Ala Val Thr Glu Asp Ser Val Ser Leu Phe Asm Gly Asm Lys> 220 210 200 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT Ile Phe Val Ser Lys Glu Lys Asn Ser Ser Gly Lys Tyr Asp Leu Arg> 270 260 250 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA Ala Thr Ile Asp Gln Val Glu Leu Lys Gly Thr Ser Asp Lys Asn Asn> . . . 320 330 310 300 290 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT Gly Ser Gly Thr Leu Glu Gly Ser Lys Pro Asp Lys Ser Lys Val Lys> 360 370 350 340 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA Leu Thr Val Ser Ala Asp Leu Asn Thr Val Thr Leu Glu Ala Phe Asp> 430 390 400 410 420

FIGURE 11 (1 of 3)

•	•		•		•	•		•		•	•		•		•
GCC	AGC	AAC	CAA	AAA	TTA	TCA	AGT	AAA	GTT	ACT	AAA	λλλ	CAG	GGG	TCA
CGG	TCG	TTG	GTT	TTT	TAA	AGT	TCA	TTT	CAA	TGA	TTT	TTT	GTC	CCC	AGT
Ala	Ser	Asn	Gln	Lvs	Ile	Ser	Ser	Lvs	Val	Thr	Lvs	Lvs	6:5	Gly	Ser>
			• • • • • • • • • • • • • • • • • • • •	-, -				-, -			-2-	_, _		Gry	3617
		140			450			4	50			170			200
	_			•				•	•						460
እጥእ	202	CAG	CVV	ACT	رسر ا	222	CCT	מ מ מ	2 2 2	لا بلعث	CAC	₩C.	***		
W Y W	TOTAL TOTAL	CTC	رين ويون	TGA.	CIC	- Carrer	CCA	ALALY VOLT	ecc.	- 174	CTC	104	P-10	***	YZA
1741	101	C1C	C11	TOA.	Lau	111	Ala	114	Yana	AAI	C16	AGI	110	117	AAT
116	ınr	GIU	GIU	1111	Dea	Lys	WIG	ASII	Lys	Leu	Asp	ser	Lys	Lys	Leu>
		49	20			00			510			٠.			
		4.	•	•	•	•		•	210		•	2.	20	_	
N C N	n C N	ጥሮ እ	3 A C	GGA	እርጥ	מים	دين	CAA	TAC		- ·	3.003		~ ~	
161	101	AG1	116	CC1	TGA	101	JAA	C11	W10	WO I	GIT	TAT	TGT	CTA	CGA
THI	AIG	ser	ASI	GIA	Inr	Inr	reu	GIU	Tyr	ser	Gin	lie	Thr	ASD	Ala>
530			540			55	: n			SED					
720		*			*	٠.	*		•				570		_
CAC	አኒጥ	CCT	A C A	AAA	GC3	CTA	CDA	» Ст	CTN	222	N N T	, cc			
CTC	ጥጥል	CCA	TOT	TTT	CCT	CAT	CUL	TCA	CIT		መጥ አ ምላ ፣	TCC	M::	446	Cir
210	111	NI a	75-	Tyr	712	CVI	C1.	7b~	t an	111	114	306	1	TTC	GAA Leu>
Asp	Mail	VIC	1 111	Lys	VIG	va.	GIU	1111	Leu	Lys	ASN	Ser	176	Lys	Leu>
5.5	80			590			600			51	LO		,	. 2 0	
٠,	•	•	•	*		•	•		•	0.	*			20	
GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	CAN	ኔ ፓፓ	222	Chi	CCT
CTT	CCT	TCA	GAA	CAT	CAG	CCT	TTT	TGT	TCT	C3C	CTT	TAA	نستند وسيحه	022	CCX
Glu	Glv	Ser	Leu	Val	Val	Glv	Lvs	The	4	Val	Glu	אנז	1	C1.	Gly>
						-	_,_	••••		141	Giu	116	Lys	حدق	Giy>
	630			64	10			550			660			57	in.
•	•		•		•	•		•		•	•		•		•
ACT	GTT	ACT	CTA	AAA	AGA	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	232	GTC
TGA	CAA	TGA	GAT	TTT	TCT	CTT	TAA	CTT	TTT	CTA	CCT	TTT	CAT	ندښله ۱۳۰۰	Cac
Thr	Val	Thr	Leu	Lys	Arg	Glu	Ile	Glu	Lvs	ASD	Glv	Lvs	Val	Lve	Val>
				_					•		,	-, -		-,-	
	. (680			690			70	00		7	710			720
•		•		•	•		•		•	•		•	•	•	*
TTT	TTG	AAT	GAC	ACT	GCA	GGT	TCT	AAC	AAA	AAA	ACA	GGT	AAA	TGG	GAA
AAA	AAC	TTA	CTG	TGA	CGT	CCA	AGA	TTG	TTT	TIT	TGT	CCA	TTT	ACC	CTT
Phe	Leu	Asn	Asp	Thr	Ala	Gly	Ser	Asn	Lys	Lys	Thr	Gly	Lys	Tro	Glu>
										_		_	•	•	
		7	30		-	740			750			76	50		
	•		•	•		• .		•	*		•		•	•	
GAC	AGT	ACT	AGC	ACT	TTA	ACA	ATT	AGT	GCT	GAC	AGC	AAA	AAA	ACT	AAA
CTG	TCA	TGA	TCG	TGA	AAT	TGT	TAA	TCA	CGA	CTG	TCG	TTT	TTT	TGA	TIT
Asp	Ser	Thr	Ser	Thr	Leu	Thr	Ile	Ser	Ala	Asp	Ser	Lys	Lys	Thr	Lys>
													•		
770			780		•	7	90		1	B00			810		
•		•	•	_	. *		•	•		•		•	•		•
GAT	TTG	GTG	TTC	TTA	ACA	GAT	GGT	ACA	TTA	ACA	GTA	CAA	CAA	TAC	AAC
CTA	AAC	CAC	AAG	TAA	TGT	CTA	CCA	TGT	TAA	TGT	CAT	GTT	GTT	ATG	TTG
Ąsp	Leu	Va1	Phe	Leu	Thr	Asp	Gly	Thr	Ile	Thr	Val	Gln	GJn	Tyr	Asn>

820 830 840 850 860

ACA GCT GGA ACC AGC CTA GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT
TGT CGA CCT TGG TCG GAT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA
Thr Ala Gly Thr Ser Leu Glu Gly Ser Ala Ser Glu Ile Lys Asn Leu>

870 880 890

*
TCA GAG CTT AAA AAC GCT TTA AAA TAA
AGT CTC GAA TTT TTG CGA AAT TTT ATT
Ser Glu Leu Lys Asn Ala Leu Lys ***>

FIGURE 11 (3 of 3)

OspC-B31 Sequence Range: 1 to 633

10	20	30	•	40
*		* *		•
ATG AAA AAG AAT	ACA TTA AGT	GCG ATA TTA	ATG ACT TTA	TTT TTA TTT
TAC TIT TIC TIA	TGT AAT TCA	CGC TAT AAT	TAC TGA AAT	AAA TAA AAA
Met Lys Lys Asn	Thr Leu Ser	Ala Ile Leu	Met Thr Leu	Phe Leu Phe>
			•	
50 60	•	70	80	90
• •	*	* *	• •	• •
ATA TOT TOT AAT	AAT TCA GGG	AAA GAT GGG	AAT ACA TCT	GCA AAT TCT
TAT AGA ACA TTA	TTA AGT CCC	TTT CTA CCC	TTA TGT AGA	CGT TTA AGA
Ile Ser Cys Asn	Asn Ser Gly	Lys Asp Giy	Asn Thr Ser	Ala Asn Ser>
	110	120	130	140
100	110 -	120	* *	*
GCT GAT GAG TCT	CTT AAA GGG	CCT AAT CTT	ACA GAA ATA	AGT AAA AAA
CGA CTA CTC AGA	CAA TTT CCC	GGA TTA GAA	TGT CTT TAT	TCA TIT TIT
Ala Asp Glu Ser	Val Lys Gly	Pro Asn Leu	Thr Glu Ile	Ser Lys Lys>
		•		
150	160	170	180	190
• •	* *	•	* *	•
ATT ACG GAT TCT				
TAA TGC CTA AGA	TTA CGC CAR	AAT GAA CGA	CAC TTT CTC	CAA CTT CGC
Ile Thr Asp Ser	Asn Ala Val	. Leu Leu Ala	Val Lys Glu	Val Glu Ala>
200	210	220	230	240
± ±	* *	* *	* *	* *
TTG CTG TCA TC	ATA GAT GA	ATT GCT GCT	AAA GCT ATT	GGT AAA AAA
AAC GAC AGT AG				
Leu Leu Ser Se				
250	260	270	2	180
* *			, m, m, m, c, c	, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,
ATA CAC CAA AA' TAT GTG GTT TT				
Ile His Gln As				•
TTE NTO OTH NO.	, 01, 20.	- 1.0p 1.1. Oz.	,	, 01, 001
290 30	0 :	310	320	330
* *	• •	• •	* •	• •
TTG TTA GCG GG	A CGT TAT GC.	A ATA TCA AC	CTA ATA AAJ	A CAA AAA TTA
AAC AAT CGC CC				
Leu Leu Ala Gl	y Arg Týr Al	a Ile Ser Th	r Leu Ile Ly:	s Gln Lys Leu>
	250	. 260	270	200
340	350	360	370	380
GAT GGA TTG A	מה מגם המג	- ב מגב בדים ב	ים חיים בגב ב	ד כרכ כרד 176
CTA CCT AAC TT				
Asp Glv Leu IA	s Asn Glu Gl			p Ala Ala Lys>

FIGURE 12 (1 of 2)

OspC-B31

420 400 390 AAA TGT TCT GAA ACA ITT ACT AAT AAA TTA AAA GAA AAA CAC ACA GAT TTT ACA AGA CTT TGT AAA TGA TTA TTT AAT TTT CTT TTT GTG TGT CTA Lys Cys Ser Glu Thr Phe Thr Asn Lys Leu Lys Glu Lys His Thr Asp> 460 470 450 480 CTT GGT AAA GAA GGT GTT ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA GAA CCA TTT CTT CCA CAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT Leu Gly Lys Glu Gly Val Thr Asp Ala Asp Ala Lys Glu Ala Ile Leu> 510 -500 AAA ACA AAT GGT ACT AAA ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TIT TGT TTA CCA TGA TTT TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT Lys Thr Asn Gly Thr Lys Thr Lys Gly Ala Glu Glu Leu Gly Lys Leu> 530 540 550 560 TTT GAA TCA GTA GAG GTC TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAA CTT AGT CAT CTC CAG AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA Phe Glu Ser Val Glu Val Leu Ser Lys Ala Ala Lys Glu Met Leu Ala> 590 600 610 580 620 AAT TCA GTT AAA GAG CTT ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA TTA AGT CAA TTT CTC GAA TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT Asn Ser Val Lys Glu Leu Thr Ser Pro Val Val Ala Glu Ser Pro Lys> 630 AAA CCT TAA TTT GGA ATT Lys Pro ***>

FIGURE 12 (2 of 2)

OspC-K48 Sequence Range: 1 to 630 22/133

			10			20			30)			40		
ATG	AAA	DAA	- ጥፈፋ:	" מרא	ጥጥል	y C.u.		• • አጥአ	لانلملة <u>*</u>	N TV	•		*		· A TTT
TAC	TTT	TTC	TTA	TGT	AAT	TCA	CGC	TAT	AAT	TAC	AC1	117 221	1111	TT	TTT A
Met	Lys	Lys	Asn	Thr	Leu	Ser	Ala	Ile	Leu	Met	Thr	Leu	Phe	I.e.	Phe>
															· rrie>
50		_	60		_		70			80			90)	
_	ىلىكلە	40Ciúi -	ግ ጥፈል	ልልጥ	- - ~~	cen	*	~~~	100	~~		*	*		•
TAT	AGA	ACA	TTA	TTA	AGT	CCA	CCC	CT3	TCC	CCT	ACA	ACI	AAT	CC	GAT
Ile	Ser	Cys	Asn	Asn	Ser	Gly	Gly	Asp	Thr	Ala	Ser	The) lin	GG/	Asp>
						-			:.		r		W211	PIC	, wab>
1	00	_	;	110			120			1.	30			140	
CNC	4.Cu	CC N		~~	~~	*	*		*		•	*		*	
CTC	AGA	CGT	dalah WWW	CCT	CCI	AAT	CTT	ACA	GTA	ATA	AGC	AAA	AAA	ATT	ACA TGT
Glu	Ser	Ala	Lys	Gly	Pro	Asn	Leu	Thr	Val	The	Ser	Tye	THE	TAA	Thr>
٠			_	_								נע	Dys	116	THE>
_	150		_	1	60		:	170			180			1	90
C ATT	س حس	יח ת ת	CCN	mmm.	*	*		. +		•	*		•		•
CTA	AGA	TTA	CCT	777	GTA	CIG	CGA	GTG	AAA	GAA	GTT	GAG	GCT	TTG	ATC TAG
Asp	Ser	Asn	Ala	Phe	Val	Leu	Ala	Val	Ivs	Glu	VA1	GIO	CGA	AAC	TAG Ile>
									-, 0		742	GIU	wra	Leu	116>
_	:	200			210			22	20		;	230			240
TCA	سحت	እጥአ *	Cam	Chh	~mm		•		•	•	_	*		•	•
AGT	AGA	TAT	CTA	CTT	CTT GAA	CCI	AAT TTA	AAA	GCT	ATT	GGT	AAA	GTA	ATA	CAT
Ser	Ser	Ile	Asp	Glu	Leu	Ala	Asn	Lvs	Ala	TAA	CLA	TIT	Val	TAT	GTA His>
				•								- 3	441	116	nis>
		2	50	_	2	60			270			28	30		
CAA	AAT	እ ል ጥ	CCT	בינה. ב	AAT	CCT.	እእጥ	*		~	*		•	•	
GTT	TTA	ATT	CCA	AAT	TTA	CGA	TTA	CCC	CCY	CAA	AAC	GGA	TCA	TTG	ATT
Gln	Asn	Asn	Gly	Leu.	Asn	Ala	Asn	Ala	Gly	Gln	Asn	GIV	Ser	Ten	Leu>
							_	•	-						Dear
290		•	300		*	31	.0		3	20			330		
GCA	GGA	GCC	TAT	GCA	ATA	TCA	ACC	СТА	ልጥል	a Ca	C 3 3	*	*	.~	*
CC1.	CCL	CGG	ATA	CGT	TAT	AGT	TGG	GAT	ጥልጥ	ALC:AL	C-12-2	CLASSALD.	3.300	AGT TCl	
Ala	Gly	Ala	Tyr	Ala	Ile	Ser	Thr	Leu	Ile	Thr	Glu	Lys	Leu	Ser	Lys>
	10											<u>-</u> ,			
	*	•	د	50		*	360		•	37	0	_	3	80	
TTG	AAA	AAT	TCA	GAA	GAG	TTA	AAT	ААА	AAA	ATT	C77	243	CCT	*	220
AAC	TII	TTA	AGT	CIT	CTC	AAT	TTA	JrTrI	بلملمك	TAA	للملت	CTC	CCA	₩ ₩	min
Leu	Lys	Asn	Ser	Glu	Glu	Leu	Asn	Lys	Lys	Ile	Glu	Glu	Ala	Lys	Asn>
		•												-	

FIGURE 13 (1 of 2)

OBPC-K48

390 400 CAT TCT GAA GCA TTT ACT AAT AGA CTA AAA GGT TCT CAT GCA CAA CTT GTA AGA CTT CGT AAA TGA TTA TCT GAT TTT CCA AGA GTA CGT GTT GAA His Ser Glu Ala Phe Thr Asn Arg Leu Lys Gly Ser His Ala Gln Leu> 450 460 470 GGA GTT GCT GCT ACT GAT GAT CAT GCA AAA GAA GCT ATT TTA AAG CCT CAA CGA CGA CGA TGA CTA CTA GTA CGT TTT CTT CGA TAA AAT TTC Gly Val Ala Ala Thr Asp Asp His Ala Lys Glu Ala Ile Leu Lys> 490 500 510 T, ==== . TCA AAT CCT ACT AAA GAT AAG GGT GCT AAA GCA CTT AAA GAC TTA TCT AGT TTA GGA TGA TTT CTA TTC CCA CGA TTT CGT GAA TTT CTG AAT AGA Ser Asn Pro Thr Lys Asp Lys Gly Ala Lys Ala Leu Lys Asp Leu Ser> 530 540 550 560 570 GAA TCA GTA GAA AGC TTG GCA AAA GCA GCG CAA GAA GCA TTA GCT AAT CTT AGT CAT CTT TCG AAC CGT TTT CGT CGC GTT CTT CGT AAT CGA TTA Glu Ser Val Glu Ser Leu Ala Lys Ala Ala Gln Glu Ala Leu Ala Asn> 590 600 610 620 * TCA GTT AAA GAA CTT ACA AAT CCT GTT GTG GCA GAA AGT CCA AAA AAA AGT CAA TTT CTT GAA TGT TTA GGA CAA CAC CGT CTT TCA GGT TTT TTT Ser Val Lys Glu Leu Thr Asn Pro Val Val Ala Glu Ser Pro Lys Lys> 630 CCT TAA GGA ATT Pro ***>

FIGURE 13 (2 of 2)

OspC-PKO Sequence Range: 1 to 639

20 ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TTT TTC TTA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA Met Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe> 50 60 80 ATA TOT TGT AGT AAT TOA GGG AAA GGT GGG GAT TOT GCA TOT ACT AAT TAT AGA ACA TCA TTA AGT CCC TTT CCA CCC CTA AGA CGT AGA TGA TTA Ile Ser Cys Ser Asn Ser Gly Lys Gly Gly Asp Ser Ala Ser Thr Asn> 100 120 110 130 CCT GCT GAC GAG TCT GCG AAA GGG CCT AAT CTT ACA GAA ATA AGC AAA GGA CGA CTG CTC AGA CGC TTT CCC GGA TTA GAA TGT CTT TAT TCG TTT Pro Ala Asp Glu Ser Ala Lys Gly Pro Asn Leu Thr Glu Ile Ser Lys> 150 160 170 180 AAA ATT ACA GAT TCT AAT GCA TTT GTA CTT GCT GTT AAA GAA GTT GAG TTT TAA TGT CTA AGA TTA CGT AAA CAT GAA CGA CAA TTT CTT CAA CTC Lys Ile Thr Asp Ser Asn Ala Phe Val Leu Ala Val Lys Glu Val Glu> 200 210 220 240 ACT TTG GTT TTA TCT ATA GAT GAA CTT GCT AAG AAA GCT ATT GGT CAA TGA AAC CAA AAT AGA TAT CTA CTT GAA CGA TTC TTT CGA TAA CCA GTT Thr Leu Val Leu Ser Ile Asp Glu Leu Ala Lys Lys Ala Ile Gly Gln> 250 260 270 AAA ATA GAC AAT AAT AAT GGT TTA GCT GCT TTA AAT AAT CAG AAT GGA TTT TAT CTG TTA TTA TTA CCA AAT CGA CGA AAT TTA TTA GTC TTA CCT-Lys Ile Asp Asn Asn Gly Leu Ala Ala Leu Asn Asn Gln Asn Gly> 290 300 310 320 330 TCG TTG TTA GCA GGA GCC TAT GCA ATA TCA ACC CTA ATA ACA GAA AAA AGC AAC AAT CGT CCT CGG ATA CGT TAT AGT TGG GAT TAT TGT CTT TTT Ser Leu Leu Ala Gly Ala Tyr Ala Ile Ser Thr Leu Ile Thr Glu Lys> 340 350 360 370. 380 TTG AGT AAA TTG AAA AAT TTA GAA GAA TTA AAG ACA GAA ATT GCA AAG AAC TCA TTT AAC TTT TTA AAT CTT CTT AAT TTC TGT CTT TAA CGT TTC Leu Ser Lys Leu Lys Asn Leu Glu Glu Leu Lys Thr Glu Ile Ala Lys>

OspC-PKO

	390		٠	40	00		4	110			420			. 43	30
•	*		•		•	•		•		•	•		•		•
CT	AAG	AAA	TGT	TCC	GAA	GAA	TTT	ACT	TAA	AAA	CTA	AAA	AGT	GGT	CAT
CGA	TTC	TTT	ACA	AGG	CTT	CTT	AAA	TGA	TTA	TTT	GAT	TTT	TCA	CCA	GTA
Ala	LVS	LVS	CVS	Ser	Glu	Glu	Phe	Thr	Asn	Lys	Leu	Lys	Ser	Gly	His>
7,20	٠,٠	_, _	-, -	-										_	
	4	140			450			46	50		4	170			480
•		•		•	•		•		•	. •		•		•	•
GCA	GAT	CTT	GGC	AAA	CAG	GAT	GCT	ACC	GAT	GAT	CAT	GCA	AAA	GCA	GCT
CGT	CTA	GAA	CCG	TTT	GTC	CTA	CGA	TGG	CTA	CTA	GTA	CGT	TTT	CGT	CGA
Ala	Asp	Leu	Gly	Lys	Gln	Asp	Ala	Thr	Asp	Asp	His	Ala	Lys	Ala	Ala>
	_								.~	-	~~ .				
		4	90		9	500			510		•	52	20		•
	•		*	*		#		•	•		•		•	•	
					GCA										
TAA	AAT	TTT	TGT	GTA	CGT	TGA	TGG	CTA	TTT	CCA	CGA	TTT	CII	AAA	TTT
Ile	Leu	Lys	Thr	His	Ala	Thr	Thr	Asp	Lys	Gly	Ala	Lys	Glu	Phe	Lys>
扩															
							5 N								
530			540			5:	50		:	560			570		
•		•	•		*		•	•	_	*		•	•		•
GAT	TTA	• TTT	GAA	TCA	* GTA	GAA	• GGT	TTG	TTA	* AAA	GCA	GCT	CAA	GTA	• GCA
GAT CTA	AAT	AAA	GAA CTT	AGT	CAT	GAA CTT	GGT CCA	AAC	ATT TAA	AAA TTT	CGT	CGA	CAA GTT	CAT	CGT
GAT CTA	AAT	AAA	GAA CTT	AGT	CAT	GAA CTT	GGT CCA	AAC	ATT TAA	AAA TTT	CGT	CGA	CAA GTT	CAT	GCA CGT Ala>
GAT CTA Asp	AAT Leu	AAA	GAA CTT Glu	AGT Ser	CAT	GAA CTT	GGT CCA Gly	AAC	ATT TAA	AAA TTT Lys	CGT	CGA	CAA GTT Gln	CAT Val	CGT
GAT CTA Asp	AAT	AAA	GAA CTT Glu	AGT	CAT	GAA CTT	GGT CCA	AAC	ATT TAA	AAA TTT Lys	CGT	CGA	CAA GTT Gln	CAT	CGT
GAT CTA Asp	AAT Leu 80	AAA Phe	GAA CTT Glu	AGT Ser 590	CAT Val	GAA CTT Glu	GGT CCA Gly	AAC Leu	TTA AAT Leu	AAA TTT Lys	CGT Ala 10	CGA Ala	CAA GTT Gln	CAT Val	CGT Ala>
GAT CTA Asp 5	AAT Leu 80 ACT	AAA Phe	GAA CTT Glu	AGT Ser 590	CAT Val	GAA CTT Glu •	GGT CCA Gly 600	AAC Leu ACA	TTA AAT Leu *	AAA TTT Lys 6:	CGT Ala 10 • GTT	CGA Ala *	CAA GTT Gln	CAT Val 20 • GAA	CGT Ala>
GAT CTA Asp 5 CTA GAT	AAT Leu 80 * ACT TGA	AAA Phe AAT TTA	GAA CTT Glu TCA AGT	AGT Ser 590 • GTT CAA	CAT Val AAA TTT	GAA CTT Glu • GAA CTT	GGT CCA Gly 600 CTT GAA	AAC Leu ACA TGT	TTA AAT Leu AGT TCA	AAA TTT Lys 6: CCT GGA	CGT Ala 10 • GTT CAA	CGA Ala * GTA CAT	CAA GTT Gln GCA CGT	CAT Val 520 GAA CTT	CGT Ala> AGT TCA
GAT CTA Asp 5 CTA GAT	AAT Leu 80 * ACT TGA	AAA Phe AAT TTA	GAA CTT Glu TCA AGT	AGT Ser 590 • GTT CAA	CAT Val AAA TTT	GAA CTT Glu • GAA CTT	GGT CCA Gly 600 CTT GAA	AAC Leu ACA TGT	TTA AAT Leu AGT TCA	AAA TTT Lys 6: CCT GGA	CGT Ala 10 • GTT CAA	CGA Ala * GTA CAT	CAA GTT Gln GCA CGT	CAT Val 520 GAA CTT	CGT Ala>
GAT CTA Asp 5 CTA GAT	AAT Leu 80 * ACT TGA Thr	AAA Phe AAT TTA	GAA CTT Glu TCA AGT	AGT Ser 590 • GTT CAA	CAT Val AAA TTT	GAA CTT Glu • GAA CTT	GGT CCA Gly 600 CTT GAA	AAC Leu ACA TGT	TTA AAT Leu AGT TCA	AAA TTT Lys 6: CCT GGA	CGT Ala 10 • GTT CAA	CGA Ala * GTA CAT	CAA GTT Gln GCA CGT	CAT Val 520 GAA CTT	CGT Ala> AGT TCA
GAT CTA Asp 5 CTA GAT	AAT Leu 80 * ACT TGA	AAA Phe AAT TTA	GAA CTT Glu TCA AGT	AGT Ser 590 • GTT CAA	CAT Val AAA TTT	GAA CTT Glu • GAA CTT	GGT CCA Gly 600 CTT GAA	AAC Leu ACA TGT	TTA AAT Leu AGT TCA	AAA TTT Lys 6: CCT GGA	CGT Ala 10 • GTT CAA	CGA Ala * GTA CAT	CAA GTT Gln GCA CGT	CAT Val 520 GAA CTT	CGT Ala> AGT TCA
GAT CTA Asp 5 CTA GAT Leu	AAT Leu 80 * ACT TGA Thr	AAA Phe AAT TTA Asn	GAA CTT Glu TCA AGT Ser	AGT Ser 590 GTT CAA Val	CAT Val AAA TTT Lys	GAA CTT Glu • GAA CTT	GGT CCA Gly 600 CTT GAA	AAC Leu ACA TGT	TTA AAT Leu AGT TCA	AAA TTT Lys 6: CCT GGA	CGT Ala 10 • GTT CAA	CGA Ala * GTA CAT	CAA GTT Gln GCA CGT	CAT Val 520 GAA CTT	CGT Ala> AGT TCA
GAT CTA Asp S CTA GAT Leu	AAT Leu 80 * ACT TGA Thr 630	AAA Phe AAT TTA Asn	GAA CTT Glu TCA AGT Ser	AGT Ser 590 • GTT CAA	CAT Val AAA TTT Lys	GAA CTT Glu • GAA CTT	GGT CCA Gly 600 CTT GAA	AAC Leu ACA TGT	TTA AAT Leu AGT TCA	AAA TTT Lys 6: CCT GGA	CGT Ala 10 • GTT CAA	CGA Ala * GTA CAT	CAA GTT Gln GCA CGT	CAT Val 520 GAA CTT	CGT Ala> AGT TCA

FIGURE 14 (2 of 2)

OspC-TRO

Sequence Range: 1 to 624

10 ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TIT TIC TIA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA Het Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe> 50 60 70 80 90 ATA TOT TGT AAT AAT TOA GGT GGG GAT TOT GCA TOT ACT AAT COT GAT TAT AGA ACA TTA TTA AGT CCA CCC CTA AGA CGT AGA TGA TTA GGA CTA Ile Ser Cys Asn Asn Ser Gly Gly Asp Ser Ala Ser Thr Asn Pro Asp> 110 120 130 140 GAG TCT GCA AAA GGA CCT AAT CTT ACC GTA ATA AGC AAA AAA ATT ACA CTC AGA CGT TTT CCT GGA TTA GAA TGG CAT TAT TCG TTT TTT TAA TGT Glu Ser Ala Lys Gly Pro Asn Leu Thr Val Ile Ser Lys Lys Ile Thr> 150 160 180 GAT TCT AAT GCA TTT TTA CTG GCT GTG AAA GAA GTT GAG GCT TTG CTT CTA AGA TTA CGT AAA AAT GAC CGA CAC TTT CTT CAA CTC CGA AAC GAA Asp Ser Asn Ala Phe Leu Leu Ala Val Lys Glu Val Glu Ala Leu Leu> 200 210 220 230 TCA TCT ATA GAT GAA CTT TCT AAA GCT ATT GGT AAA AAA ATA AAA AAT AGT AGA TAT CTA CTT GAA AGA TTT CGA TAA CCA TTT TTT TAT TTT TTA Ser Ser Ile Asp Glu Leu Ser Lys Ala Ile Gly Lys Lys Ile Lys Asn> 250 260 270 GAT GGT ACT TTA GAT AAC GAA GCA AAT CGA AAC GAA TCA TTG ATA GCA CTA CCA TGA AAT CTA TTG CTT CGT TTA GCT TTG CTT AGT AAC TAT CGT Asp Gly Thr Leu Asp Asn Glu Ala Asn Arg Asn Glu Ser Leu Ile Ala> 310 320 330 GGA GCT TAT GAA ATA TCA AAA CTA ATA ACA CAA AAA TTA AGT GTA TTG CCT CGA ATA CTT TAT AGT TTT GAT TAT TGT GTT TTT AAT TCA CAT AAC Gly Ala Tyr Glu Ile Ser Lys Leu Ile Thr Gln Lys Leu Ser Val Leu> 340 350 360 370 .380 AAT TCA GAA GAA TTA AAG AAA AAA ATT AAA GAG GCT AAG GAT TGT TCC TTA AGT CTT CTT AAT TTC TTT TTT TAA TTT CTC CGA TTC CTA ACA AGG Asn Ser Glu Glu Leu Lys Lys Lys Ile Lys Glu Ala Lys Asp Cys Ser>

OspC-TRO

	390			40	00		4	110			420			4	30
•	•	•	*		•	•		•		•	•		. •		•
GAA	AAA	TTT	ACT	ACT	AAG	CTA	AAA	GAT	AGT	CAT	GCA	GAG	CTT	GGT	ATA
CTT	TTT	AAA	TGA	TGA	TTC	GAT	TTT	CTA	TCA	GTA	CGT	CTC	GAA	CCA	TAT
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CAA	AGC	GTT	CAG	GAT	GAT	AAT	GCA	AAA	AAA	GCT	ATT	TTA	AAA	ACA	CAT
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GGA	ACT	AAA	GAC	AAG	GGT	GCT	AAA	GAA	CTT	GAA	GAG	TTA	TTT	AAA	TCA
															AGT
															Ser>
013		, -					•						-	-3-	
530			540			55	50		9	560			570		
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CTA	GAA	AGC	TTG	TCA	AAA	GCA	GCG	CAA	GCA	GCA	TTA	ACT	AAT	TCA	GII
GAT	CTT	TCG	AAC	AGT	TTT	CGT	CGC	GTT	CGT	CGT	AAT	TGA	TTA	AGT	CAA
Leu	Glu	Ser	Leu	Ser	Lys	Ala	Ala	Gln	Ala	Ala	Leu	Thr	Asn	Ser	Val>
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51	30			590			600			61	LO		6	520	
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AAA	GAG	CTT	ACA	AAT	CCT	GTT	GTG	GCA	GAA	AGT	CCA	AAA	AAA	CCT	TAA
TIT	CTC	GAA	TGT	TTA	GGA	CAA	CAC	CGT	CTT	TCA	GGT	TTT	TIT	GGA	TTA
Lys	Glu	Leu	Thr	Asn	Pro	Val	Val	Ala	Glu	Ser	Pro	Lys	Lys	Pro	***>

FIGURE 15 (2 of 2)

P93

Sequence Range: 1 to 2102

30 ATG AAA AAA ATG TTA CTA ATC TTT AGT TTT TTT CTT ATT TTC TTG AAT TAC TIT TIT TAC AAT GAT TAG AAA TCA AAA AAA GAA TAA AAG AAC TTA Met Lys Lys Met Leu Leu Ile Phe Ser Phe Phe Leu Ile Phe Leu Asn> 80 60 70 50 GGA TIT CCT GTT AGT GCA AGA GAA GTT GAT AGG GAA AAA TTA AAG GAC CCT AAA GGA CAA TCA CGT TCT CTT CAA CTA TGG-CTT TTT AAT TTC CTG Gly Phe Pro Val Ser Ala Arg Glu Val Asp Arg Glu Lys Leu Lys Asp> - 120 130 110 100 TTT GTT AAT ATG GAT CTT GAG TTT GTA AAT TAT AAA GGC CCT TAT GAT AAA CAA TTA TAC CTA GAA CTC : A CAT TTA ATA TTT CCG GGA ATA CTA Phe Val Asn Met Asp Leu Glu Phe Val Asn Tyr Lys Gly Pro Tyr Asp> 170 180 160 TCT ACA AAT ACA TAT GAA CAA ATA GTG GGT ATT GGG GAG TTT TTA GCA AGA TGT TTA TGT ATA CTT GTT TAT CAC CCA TAA CCC CTC AAA AAT CGT Ser Thr Asn Thr Tyr Glu Gln Ile Val Gly Ile Gly Glu Phe Leu Ala> 210 220 230 240 AGA CCG TTG ACC AAT TCC AAT AGC AAC TCA AGT TAT TAT GGT AAA TAT TCT GGC AAC TGG TTA AGG TTA TCG TTG AGT TCA ATA ATA CCA TTT ATA Arg Pro Leu Thr Asn Ser Asn Ser Asn Ser Ser Tyr Tyr Gly Lys Tyr> 270 280 250 TTT ATT AAT AGA TTT ATT GAT GAT CAA GAT AAA AAA GCA AGC GTT GAT AAA TAA TTA TCT AAA TAA CTA CTA GTT CTA TTT TTT CGT TCG CAA CTA Phe Ile Asn Arg Phe Ile Asp Asp Gln Asp Lys Lys Ala Ser Val Asp> 330 320 300 310 290 GTT TTT TCT ATT GGT AGT AAG TCA GAG CTT GAC AGT ATA TTG AAT TTA CAA AAA AGA TAA CCA TCA TTC AGT CTC GAA CTG TCA TAT AAC TTA AAT Val Phe Ser Ile Gly Ser Lys Ser Glu Leu Asp Ser Ile Leu Asn Leu> 380 360 370 340 350 AGA AGA ATT CTT ACA GGG TAT TTA ATA AAG TCT TTC GAT TAT GAC AGG TCT TCT TAA GAA TGT CCC ATA AAT TAT TTC AGA AAG CTA ATA CTG TCC Arg Arg Ile Leu Thr Gly Tyr Leu Ile Lys Ser Phe Asp Tyr Asp Arg>

FIGURE 16 (1 of 5)

390 400 420 TCT AGT GCA GAA TTA ATT GCT AAG GTT ATT ACA ATA TAT AAT GCT GTT AGA TCA CGT CTT AAT TAA CGA TTC CAA TAA TGT TAT ATA TTA CGA CAA Ser Ser Ala Glu Leu Ile Ala Lys Val Ile Thr Ile Tyr Asn Ala Val> 440 450 460 470 TAT AGA GGA GAT TTG GAT TAT TAT AAA GGG TTT TAT ATT GAG GCT GCT ATA TCT CCT CTA AAC CTA ATA ATA TTT CCC AAA ATA TAA CTC CGA CGA Tyr Arg Gly Asp Leu Asp Tyr Tyr Lys Gly Phe Tyr Ile Glu Ala Ala> 500 510 . . = .= . TTA AAG TCT TTA AGT AAA GAA AAT GCA GGT CTT TCT AGG GTT TAT AGT AAT TTC AGA AAT TCA TTT CTT TTA CGT CCA GAA AGA TCC CAA ATA TCA Leu Lys Ser Leu Ser Lys Glu Asn Ala Gly Leu Ser Arg Val Tyr Ser> 540 550 560 CAG TGG GCT GGA AAG ACA CAA ATA TTT ATT CCT CTT AAA AAG GAT ATT GTC ACC CGA CCT TTC TGT GTT TAT AAA TAA GGA GAA TTT TTC CTA TAA Gln Trp Ala Gly Lys Thr Gln Ile Phe Ile Pro Leu Lys Lys Asp Ile> 580 590 600 610 TTG TCT GGA AAT ATT GAG TCT GAC ATT GAT ATT GAC AGT TTA GTT ACA AAC AGA CCT TTA TAA CTC AGA CTG TAA CTA TAA CTG TCA AAT CAA TGT Leu Ser Gly Asn Ile Glu Ser Asp Ile Asp Ile Asp Ser Leu Val Thr> 630 640 650 €€0 GAT AAG GTG GTG GCA GCT CTT TTA AGT GAA AAT GAA GCA GGT GTT AAC CTA TTC CAC CAC CGT CGA GAA AAT TCA CTT TTA CTT CGT CCA CAA TTG Asp Lys Val Val Ala Ala Leu Leu Ser Glu Asn Glu Ala Gly Val Asn> 690 700710 680 TTT GCA AGA GAT ATT ACA GAT ATT CAA GGC GAA ACT CAT AAG GCA GAT AAA CGT TCT CTA TAA TGT CTA TAA GTT CCG CTT TGA GTA TTC CGT CTA Phe Ala Arg Asp Ile Thr Asp Ile Gln Gly Glu Thr His Lys Ala Asp> 740 750 CAA GAT AAA ATT GAT ATT GAA TTA GAC AAT ATT CAT GAA AGT GAT TCC GTT CTA TTT TAA CTA TAA CTT AAT CTG TTA TAA GTA CTT TCA CTA AGG Gln Asp Lys Ile Asp Ile Glu Leu Asp Asn Ile His Glu Ser Asp Ser> 780 790 800 AAT ATA ACA GAA ACT ATT GAA AAT TTA AGG GAT CAG CTT GAA AAA GCT TTA TAT TGT CTT TGA TAA CTT TTA AAT TCC CTA GTC GAA CTT TTT CGA Asn Ile Thr Glu Thr Ile Glu Asn Leu Arg Asp Gln Leu Glu Lys Ale>

FIGURE 16 (2 of 5)

820 830 850 860 ACA GAT GAA GAG CAT AAA AAA GAG ATT GAA AGT CAG GTT GAT GCT AAA TGT CTA CTT CTC GTA TTT TTT CTC TAA CTT TCA GTC CAA CTA CGA TTT Thr Asp Glu Glu His Lys Lys Glu Ile Glu Ser Gln Val Asp Ala Lys> 870 880 890 900 AAG AAA CAA AAG GAA GAG CTA GAT AAA AAG GCA ATA AAT CTT GAT AAA TTC TTT GTT TTC CTT CTC GAT CTA TTT TTC CGT TAT TTA GAA CTA TTT Lys Lys Gln Lys Glu Glu Leu Asp Lys Lys Ala Ile Asn Leu Asp Lys> 920 930 940 950 GCT CAG CAA AAA TTA GAT TCT GCT GAA GAT AAT TTA GAT GTT CAA AGA CGA GTC GTT TTT AAT CTA AGA CGA CTT CTA TTA AAT CTA CAA GTT TCT Ala Gln Gln Lys Leu Asp Ser Ala Glu Asp Asn Leu Asp Val Gln Arg> 970 980 990 AAT ACT GTT AGA GAG AAA ATT CAA GAG GAT ATT AAC GAA ATT AAC AAG TTA TGA CAA TCT CTC TTT TAA GTT CTC CTA TAA TTG CTT TAA TTG TTC Asn Thr Val Arg Glu Lys Ile Gln Glu Asp Ile Asn Glu Ile Asn Lys> 1020 1030 1040 1050 GAA AAG AAT TTA CCA AAG CCT GGT GAT GTA AGT TCT CCT AAA GTT GAT CTT TTC TTA AAT GGT TTC GGA CCA CTA CAT TCA AGA GGA TTT CAA CTA Glu Lys Asn Leu Pro Lys Pro Gly Asp Val Ser Ser Pro Lys Val Asp> 1070 1080 1090 1100 AAG CAA CTA CAA ATA AAA GAG AGC CTG GAA GAT TTG CAG GAG CAG CTT TTC GTT GAT GTT TAT TTT CTC TCG GAC CTT CTA AAC GTC CTC GTC GAA Lys Gln Leu Gln Ile Lys Glu Ser Leu Glu Asp Leu Gln Glu Gln Leu> 1110 1120 1130 1140 AAA GAA ACT GGT GAT GAA AAT CAG AAA AGA GAA ATT GAA AAG CAA ATT TTT CTT TGA CCA CTA CTT TTA GTC TTT TCT CTT TAA CTT TTC GTT TAA Lys Glu Thr Gly Asp Glu Asn Gln Lys Arg Glu Ile Glu Lys Gln Ile> 1160 1170 1180 1190 GAA ATC AAA AAA AGT GAT GAA AAG CTT TTA AAA AGT AAA GAT GAT AAA CTT TAG TIT TTT TCA CTA CTT TTC GAA AAT TTT TCA TTT CTA CTA TTT Glu Ile Lys Lys Ser Asp Glu Lys Leu Leu Lys Ser Lys Asp Asp Lys> 1220 1230 GCA AGT AAA GAT GGT AAA GCC TTG GAT CTT GAT CGA GAA TTA AAT TCT CGT TCA TTT CTA CCA TTT CGG AAC CTA GAA CTA GCT CTT AAT TTA AGA Ala Ser Lys Asp Gly Lys Ala Leu Asp Leu Asp Arg Glu Leu Asn Ser>

FIGURE 16 (3 of 5)

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1290 1280 1260 1250 AAA GCT TCT AGC AAA GAA AAA AGT AAA GCC AAG GAA GAA ATA ACC TTT CGA AGA TCG TTT CTT TTT TCA TTT CGG TTC CTT CTT TAT TGG Lys Ala Ser Ser Lys Glu Lys Ser Lys Ala Lys Glu Glu Glu Ile Thr> 1330 1320 1310 AAG GGT AAG TCA CAG AAA AGC TTA GGC GAT TTG AAT AAT GAT GAA AAT TTC CCA TTC AGT GTC TTT TCG AAT CCG CTA AAC TTA TTA CTA CTT TTA Lys Gly Lys Ser Gln Lys Ser Leu Gly Asp Leu Asn Asn Asp Glu Asn> 1370 - -- 1380 1360 1350 CTT ATG ATG CCA GAA GAT CAA AAA TTA CCT GAG GTT AAA AAA TTA GAT GAA TAC TAC GGT CTT CTA GTT TTT AAT GGA CTC CAA TTT TTT AAT CTA Leu Met Met Pro Glu Asp Gln Lys Leu Pro Glu Val Lys Lys Leu Asp> 1430 1420 1410 1400 AGC AAA AAA GAA TTT AAA CCT GTT TCT GAG GTT GAG AAA TTA GAT AAG TCG TTT TTT CTT AAA TTT GGA CAA AGA CTC CAA CTC TTT AAT CTA TTC Ser Lys Lys Glu Phe Lys Pro Val Ser Glu Val Glu Lys Leu Asp Lys> 1470 1460 1450 ATT TTC AAG TCT AAT AAC AAT GTT GGA GAA TTA TCA CCG TTA GAT AAA TAA AAG TTC AGA TTA TTG TTA CAA CCT CTT AAT AGT GGC AAT CTA TTT Ile Phe Lys Ser Asn Asn Asn Val Gly Glu Leu Ser Pro Leu Asp Lys> 1520 1510 1490 1500 TCT TCT TAT AAA GAC ATT GAT TCA AAA GAG GAG ACA GTT AAT AAA GAT AGA AGA ATA TTT CTG TAA CTA AGT TTT CTC CTC TGT CAA TTA TTT CTA Ser Ser Tyr Lys Asp Ile Asp Ser Lys Glu Glu Thr Val Asn Lys Asp> 1550 1560 1570 GTT AAT TTG CAA AAG ACT AAG CCT CAG GTT AAA GAC CAA GTT ACT TCT CAA TTA AAC GTT TTC TGA TTC GGA GTC CAA TTT CTG GTT CAA TGA AGA Val Asn Leu Gln Lys Thr Lys Pro Gln Val Lys Asp Gln Val Thr Ser> 1620 1600 1610 1590 TTG AAT GAA GAT TTG ACT ACT ATG TCT ATA GAT TCC AGT AGT CCT GTA AAC TTA CTT CTA AAC TGA TGA TAC AGA TAT CTA AGG TCA TCA GGA CAT Leu Asn Glu Asp Leu Thr Thr Met Ser Ile Asp Ser Ser Ser Pro Val> 1670 1660 1650 1640 TTT TTA GAG GTT ATT GAT CCA ATT ACA AAT TTA GGA ACT CTT CAA CTT AAA AAT CTC CAA TAA CTA GGT TAA TGT TTA AAT CCT TGA GAA GTT GAA Phe Leu Glu Val Ile Asp Pro Ile Thr Asn Leu Gly Thr Leu Gln Leu>

FIGURE 16 (4 of 5)

1720 1690 1700 ATT GAT TTA AAT ACT GGT GTT AGG CTT AAA GAA AGC ACT CAG CAA GGC TAA CTA AAT TTA TGA CCA CAA TCC GAA TTT CTT TCG TGA GTC GTT CCG Ile Asp Leu Asn Thr Gly Val Arg Leu Lys Glu Ser Thr Gln Gln Gly> 1750 1760 1740 1730 ATT CAG CGG TAT GGA ATT TAT GAA CGT GAA AAA GAT TTG GTT GTT ATT TAA GTC GCC ATA CCT TAA ATA CTT GCA CTT TTT CTA AAC CAA CAA TAA Ile Glm Arg Tyr Gly Ile Tyr Glu Arg Glu Lys Asp Leu Val Val Ile> 1790 1800 1780 AAA ATG GAT TCA GGA AAA GCT AAG CTT CAG ATA CTT GAT AAA CTT GAA TTT TAC CTA AGT CCT TTT CGA TTC GAA GTC TAT GAA CTA TTT GAA CTT Lys Met Asp Ser Gly Lys Ala Lys Leu Gln Ile Leu Asp Lys Leu Glu> 1850 1860 1840 1870 1830 AAT TTA AAA GTG GTA TCA GAG TCT AAT TTT GAG ATT AAT AAA AAT TCA TTA AAT TTT CAC CAT AGT CTC AGA TTA AAA CTC TAA TTA TTT TTA AGT Asn Leu Lys Val Val Ser Glu Ser Asn Phe Glu Ile Asn Lys Asn Ser> 1880 1890 1900 1910 1920 TCT CTT TAT GTT GAT TCT AAA ATG ATT TTA GTA GCT GTT AGG GAT AAA AGA GAA ATA CAA CTA AGA TTT TAC TAA AAT CAT CGA CAA TCC CTA TTT Ser Leu Tyr Val Asp Ser Lys Met Ile Leu Val Ala Val Arg Asp Lys> 1940 1950 1960 1930 GAT AGT AGT AAT GAT TGG AGA TTG GCC AAA TTT TCT CCT AAA AAT TTA CTA TCA TCA TTA CTA ACC TCT AAC CGG TTT AAA AGA GGA TTT TTA AAT Asp Ser Ser Asn Asp Trp Arg Leu Ala Lys Phe Ser Pro Lys Asn Leu> 1980 1990 2000 2010 • • GAT GAG TTT ATT CTT TCA GAG AAT AAA ATT ATG CCT TTT ACT AGC TTT CTA CTC AAA TAA GAA AGT CTC TTA TTT TAA TAC GGA AAA TGA TCG AAA Asp Glu Phe Ile Leu Ser Glu Asn Lys Ile Met Pro Phe Thr Ser Phe> 2060 2040 2050 2030 2020 TCT GTG AGA AAA AAT TTT ATT TAT TTG CAA GAT GAG TTT AAA AGT CTA AGA CAC TCT TTT TTA AAA TAA ATA AAC GTT CTA CTC AAA TTT TCA GAT Ser Val Arg Lys Asn Phe Ile Tyr Leu Gln Asp Glu Phe Lys Ser Leu> 2080 2090 2100 2070 GTT ATT TTA GAT GTA AAT ACT TTA AAA AAA GTT AAG TA CAA TAA AAT CTA CAT TTA TGA AAT TTT TTT CAA TTC AT Val Ile Leu Asp Val Asn Thr Leu Lys Lys Val Lys Xxx>

FIGURE 16 (5 of 5)

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1	ATGAAAAAAT	TGTTACTAAT	CTTTAGTTTT	TTTCTTATTT	CTTTGAATGG	ATTICCICIT
61	AATTCAAGGG	AAGTTGATAA	GGAAAAATTA	AAGGATTTTG	TTAATATGGA	TCTTGAGTTT
121	GTAAACTATA	AAGGTCCTTA	TGATTCTACA	AATACATATG	AACAAATAGT	AGSTATTGGT
181	GAGTTTTTAG	CAAGACCATT	GATTAATTCC	AATAGCAACT	CAATTTATTA	TGGTAAATAT
241	ATAATTATTT	GATTTATTGA	TGATCAAGAT	AAAAAAGCAA	GCGTTGATGT	TITITCTATT
301	GGTAGTAGGT	CACAGCTTGA	CAGTATATTG	AATCTAAGAA	GAATTCTTAC	AGGGTATTTG
361	ATARAGTCTT	TTGATTATGA	AAGATCTAGT	GCTGAATTAA	TTGCTAAGGT	TATTACAATA
421	CATAATGCTG	TTTATAGAGG	GGATTTAAAT	TATTATAAAG	AGGTTTATAT	TGAGGCTGCT
481	TTDAAGTCTT	TAACTAAAGA	AAATGCAGGT	CTTTCTAGAG	TGTACAGTCA	ATGGGCTGGA
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTTAT	CTGGAAAAGT	TGAGTCTGAC
601	ATTGATATTG	ACAGTTTGGT	TACAGATAAG	GTTGTGGCAG	-CTCTTTTAAG	CGAGAATGAA
661	GCAGGTGTTA	ACTITICAAG	AGATATTACA	GATATTCAAG	GCGAAACTCA	TAAAGCAGAT
721	CAAGATAAAA	TTGATATTGA	ATTAGATAAT	GTTCATAAAA	GTGATTCCAA	TATAACAGAG
781	ACTATTGAGA	ATTTAAGAGA	TCAGCTTGAA	AAGGCTACAG	ATGAAGAGCA	TAGAAAAGAG
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAAGAAG	AACTAGATAA	AAAGGCAATC
901	GATCTTGATA	AAGCCCAACA	AAAATTAGAT	TCTTCTGAAG	ATAATTTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGAT	TCAAGAGGAT	ATTGACGAGA	TTAATAAAGA	AAAGAATTTG
1021	CCAAAACCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AGCTACAAAT	AAAAGAGAGT
1081	CTAGAAGACT	TGCAGGAACA	GCTTAAAGAA	ACTAGCGATG	AAAATCAAAA	AAGAGAAATT
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAGTGAT	GAAGAACTTT	TAAAAAGTAA	AGATCCTAAA
1201	GCATTAGATC	TTAATGGAGA	TTTAAATTCT	AAAGTTTCTA	GTAAAGAAAA	AATTAAAGGC
1261	AAAGAAGGAG	AAATAGTCAA	AGAGGAATCA	AAGGCAAGTT	TAGCTGATTT	GAATAATGAC
1321	GAAAATCTTA	TGAGGCCGGA	AGATCAAAAA	TTATCTGAGG	TTAAAAATT	AGATAGTAAA
1381	AATTTAA	AACCTGTTTC	TGAGATTGAG	AGAGTAAATG	AAATTTCGAA	GTCTAACAAC
1441	AATGAGATTA	GTGAATCATC	ACCATTATAT	AAGCCTTCTT	ATAGCGATAT	GGATTCAAAA
	GAGGGTATAG					
1561	CCTACTTCTT					
1621		TTGATCCTAT				
	GGTGTTAGAC					
	GAAAAAGATT					
	AAACTTGAGA					
1861	CTTTATGTTG	ACTCTAAAAT	GATTTTAGTA	GTTGTGAGAG	ATAGTGGTAA	TGTTTGGAGA
	TIGGCTAAAT					
	CCTTTTACTA					GTTTAAAAGT
2041	CTTATTACTT	TAGATGTAAA	TACTTTAAAA	AAAGTTAAGT	A	

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_1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TITCTTGTTT	TTTTAAATGG	White Male Walter
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141	GITAATTACA	AGGGTCCTTA	TGATTCTACA	GATACATATY	ውን ለጥል ፈ ባፈ ፈ	A COMP mmone
181	GAGTTTTTAG	CAAGGCCGTT	GAACAATTCC	AATAGTAATT	لاستدلاشت والأرا	TYCOTA A A MAM
241	TITGITAATA	GATITATIGA	CGATCAAGAT	AAAAAAACCAA	Cutations and an	
301	GGTAGTAAGT	CAGAGCTIGA	TAGTATATTA	AATCTAACAA	Cy y and Court of Co.	3.000
361	ATGAAGICIT	TIGATTATGA	GAGGTCTAGT	GCGGAATTAA	TICCTADACC	ALY MAILY CON P WAS
421	TATAATGCTG	TITATAGAGG	AGATTTAGAT	TATTACAAAC	y Calabalaty us w	mas access
481	TIGAAGICIT	TGACTAAAGA	AAATGCAGGT	CLIMATANACCO	מרשיים הארשיים	100000000
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	to Votatatato Value V	CTCCXXXTCC	mas a
601	ATTGATATTG	ATAGTTTGGT	TACAGATAAG	GTGGTGGCAG	CIGGRAMICI	TGAGTCTGAC
661	TCAGGTGTTA	ACTITICAAG	AGATATTACA	GACATTCAAG	CCCSSSCOOL	TGAGAATGAA
721	CAAGATAAAA	TIGATATICA	ארדאה אדע איז	TTTCATGAAA	GCGAAACICA	TAAAGCAGAT
781	ACTATTGAGA	ATTTAAGGGA	TCACCTTCAA	AAAGCTACAG	GIGATICCAA	TATAACAGAA
841	ATTGAAAGTC	ACCTTCATCC	TAAAAACAAA	CAAAAGGAAG	ATGAAGAGCA	TAAAAAAGAG
901	GATCTTGATA	AAGCTCAACA	מבושנים משונה מממ	TTTGCTGAAG	AATTAGATAA	AAAGGCAATT
961	GATACTCTTA	GAGAGAAGCT	TCDDCDDDT	ATTAACGAGA	ATAATCTAGA	TATTCAAAGG
1021	CCAAAGCCTG	CTCATCTAAC	Terronania I	GTTGATAAGC	CIAATAAGGA	AAAGAATITA
1081	CTAGAAGATT	TGCAAGAGCA	CCTTALACAA	GCTAGTGATG	AGTIGCAGAT	AAAAGAGAGT
1141	GAAAAGCAAA	TTCALATCAL	מתכתו מל מל מל	GAAGAACTTT	AAAATCAAAA	aagagaaata
1201	GCATTAGATC	TTAAGCAAGA	July 2 Value	AAAGCTTCTA	TTAAAAATAA	AGATCATAAA
1261	GAAGAAGAGG	ATAAACAATT	ACATACTANA	AAAAATTTAG	GTAAAGAAAA	AATTGAAGGC
1321	AAAGTAGATA	AAATTTCAA	CTCTANCANC	AATGAGGTTA	AGCCTGTTTC	TGAGGCTGAT
1381	CYCCLIALAL	ATACCOCACAT	OLCINICANC	MAIGAGGTTA	GTAAATTATC	CCCGTTAGAT
1441	CAAAAAACTA	ATACCOACAI	TCA A A CTOCA A	GAGGGTGTAG CCTACTTCGT	ATAACAAAGA	TGTTGATTTG
1501	CTCTCTPATAC	MACCCCCTO 7	TOWARDI CAM	CCTACTTCGT	TAAATGAAGA	TTTGATTGAT
1561	CCAACCCTTC	VITCOURING	TCCTGTCTTT	TTAGAGGTTA	TCGATCCGAT	TACAAATTTA
1621	CCTATTCACC	CATATOCAAT	TITGAATACC	GGTGTTAGAC	TTAAAGAAAG	TGCTCAACAA
1681	TCACCAAAAC	CLY Y COLLICY	CAMACGI	GAAAAAGATT	TGGTTGTTAT '	TAAAATAGAT
1741	TOTOGRAPHIC	CIMAGCIICA	GATACTIGAT	AAACTCGAGA	ATTTAAAAGT	GATATCAGAG
1801	7/10011110	MUMITANIAA	AAATTI ATY	- Article Kutoteta	10000000000	
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-201	PUVOT TWWOT.	Α ,				

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	201	VGIVOIVAGI		CACTIATIATITY	א איז א נוואואוים פ	C \ \ MM \	
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		410001011	TOWLINANGA	AAAHTI ACIT	· CALEDALANS ON V	MORA 01	
	541	AAGACACAAA	TATTTATTCC	TOTTALLE	AATATTTTAT	TGTACAGTCA	ATGGGCTGGA
	601	ATTGATATTG	ATACTITICAT	TACACATAAC	GTTGTGGCAG	CIGGAAAAAT	TGAGTCTGAC
	661	GCAGGTGTTA	ACTITICANO	CCDADAADACA	GATATTCAAG	CICITITAAG	CGAAAATGAA
	721	CAAGATAAAA	TTCATATTCA	DOMINITACE OF THE PROPERTY OF	GATATTCAAG	GAGAAACTCA	TAAAGCAGAT
	781	ACTATICACA	ATTENDACTOR	WATTAGATAAT	GTTCATGAAA	GTGATTCCAA	TATAACAGAA
	841	ATTGAAACTC	WATE TANGENGY	TCAGCTTGAA	AAGGCTACAG	ATGAAGAGCA	TAGAAAAGAG
	901	CATCATTACATA	MOTIONIC.	1 MAMAMAGAAA	CAAAAAGAAG	AACTAGATAA	AAAGGCAATC
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		CCARACCIO	CILCALIANI	1 11 11 1 1 1 1 1 1		10000000	
							AUGUNTITIG
	2041.	CITATTACTT	TAGATGTAAA	TACTTTAAAA	AAAGTTAAGT	A ·	OIIIMAAAGI
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1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TITCITGITI	TTTTAAATGG	ATTTCCTCTT
61	AATGCAAGGG					
121				AATACATATG		
181						
241	TTTGTTAATA	GATTTATTGA	CGATCAAGAT	AAAAAAGCAA	GTGTTGATAT	TTTTTCTATT
301	GGTAGTAAGT	CAGAGCTTGA	TAGTATATTA	AATCTAAGAA	GAATTCTTAC	AGGGTATTTA
361				GCGGAATTAA		
421				TATTACAAAG		
481				CTTTCTAGGG		
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTTAT	CIGGAAATGI	TGAGTCTGAC
601				GTGGTGGÇAG		
661				GACATTCAAG		
721	CAAGATAAAA					
781						
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAGGAAG	AATTAGATAA	AAAGGCAATT
901	GATCTTGATA	AAGCTCAACA	AAAATTAGAT	TTTGCTGAAG	ATAATCTAGA	TATTCAAAGG
961				ATTAACGAGA		
1021	CCAAAGCCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AACTACAAAT	AAAAGAGAGC
1081				ACTGGTGATG		
1141				GAAAAGCTTT		
1201				GATCGAGAAT		
1261				ATAACCAAGG		
1321				ATGCCAGAAG		
1381				CCTGTTTCTG		
1441				TTATCACCGT		
1501	GACATTGATT	CAAAAGAGGA	GACAGTTAAT	AAAGATGTTA	ATTTGCAAAA	GACTAAGCCT
1561	CAGGTTAAAG	ACCAAGTTAC	TTCTTTGAAT	GAAGATTTGA	CTACTATGTC	TATAGATTCC
1621	AGTAGTCCTG	TATTTTTAGA	GGTTATTGAT	CCAATTACAA	ATTTAGGAAC	TCTTCAACTT
1681	ATTGATTTAA	ATACTGGTGT	TAGGCTTAAA	GAAAGCACTC	AGCAAGGCAT	TCAGCGGTAT
1741	GGAATTTATG	AACGTGAAAA	AGATTTGGTT	GTTATTAAAA	TGGATTCAGG	AAAAGCTAAG
1801	CTTCAGATAC	TTGATAAACT	TGAAAATTTA	AAAGTGGTAT	CAGAGTCTAA	TTTTGAGATT
	TTAAAAATA					
1921				TITTCTCCTA		
1981	CTTTCAGAGA	TATRAAATA	GCCTTTTACT	AGCTTTTCTG	TGAGAAAAA	TATITATITAT
2041		AGTITAAAAG	TCTAGTTATT	TTAGATGTAA	ATACTTTAAA	AAAAGTTAAG
2101	TAAAGCC					

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	ATGAAAAAA					
	AATGCAAGGG					
	GTTAATTACA					
	GAGTTTTTAG					
	TTTGTTAATA					
	GGTAGTAAGT					
361						TATTACAATA
421	TATAATGCTG	TTTATAGAGG	AGATTTAGAT	TATTACAAAG	AGTTTTATAT	TGAGGCTTCT
481	TIGAAGICIT	TGACTAAAGA	AAATGCAGGT	CTTTCTAGGG	TGTACAGTCA	ATGGGCTGGG
	AAGACACAAA					
601	ATTGATATTG	ATAGTTTGGT	TACAGATAAG	GTGGTGGCAG	CICTITIAAG	TGAGAATGAA
661	TCAGGTGTTA	ACTITGCAAG	AGATATTACA	GACATTCAAG	GCGAAACTCA	TAAAGCAGAT
	CAAGATAAAA					
781	ACTATTGAGA	ATTTAAGGGA	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	TAAAAAAGAG
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAGGAAG	AATTAGATAA	AAAGGCAATT
901	GATCTTGATA	AAGCTCAACA	AAAATTAGAT	TTTGCTGAAG	ATAATCTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGCT	TCAAGAAAAT	ATTAACGAGA	CTAATAAGGA	AAAGAATTTA
1021	CCAAAGCCTG	GTGATGTAAG	TTCTCCTAAG	GTTGATAAGC	AGTTGCAGAT	AAAAGAGAGT
1081	CTAGAAGATT	TGCAAGAGCA	GCTTAAAGAA	GCTAGTGATG	AAAATCAAAA	AAGAGAAATA
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAATGAT	GAAGAACTTT	AATAAAATT	AGATCATAAA
1201	GCATTAGATC	TTAAGCAAGA	ATTAAATTCT	AAAGCTTCTA	GTAAAGAAAA	AATTGAAGGC
1261	GAAGAAGAGG	ATAAAGAATT	AGATAGTAAA	AAAAATTTAG	AGCCTGTTTC	TGAGGCTGAT
1321	AAAGTAGATA	AAATTTCCAA	GTCTAACAAC	AATGAGGTTA	GTAAATTATC	CCCGTTAGAT
1381	GAGCCTTCTT	ATAGCGACAT	TGATTCGAAA	GAGGGTGTAG	ATAACAAAGA	TGTTGATTTG
1441	CAAAAAACTA	AACCCCAAGT	TGAAAGTCAA	CCTACTTCGT	TAAATGAAGA	CTTGATTGAT
1501	GTGTCTATAG	ATTCCAGTAA	TCCTGTCTTT	TTAGAGGTTA	TCGATCCGAT	TACAAATTTA
1561	GGAACGCTTC	AACTTATTGA	TTTGAATACC	GGTGTTAGAC	TTAAAGAAAG	TGCTCAACAA
1621.	GGTATTCAGC	GATATGGAAT	TTATGAACGT	GAAAAAGATT	TEGTTETTAT	TAAAATAGAT
1681	TCAGGAAAAG	CTAAGCTTCA	GATACTTGAT	AAACTCGAGA	ATTTAAAAGT	GATATCAGAG
1741	TCTAATTTTG	AGATTAATAA	AAATTCATCT	CTTTATGTTG	ACTCTAGAAT	GATTTTAGTA
1801	GTTGTTAAGG	ACGATAGTAA	TGCTTGGAGA	TTGGCTAAAT	TTTCTCCTAA	AAATTTAGAT
1891	GAATTTATTC	TGTCAGAAAA	TAAAATTTTG	CCTTTTACTA	GCTTTGCTGT	GAGAAAGAAT
1921	TTTATTTATT	TGCAAGATGA	ACTTAAAAGC	TTAGTTACTT	TAGATGTAAA	TACTTTAAAA
1981	AAAGTTAAGT	A		-		

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1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TTTCTTATTT	TTTTGAATGG	ATTTCCTCTT
61	AATCCAAGGA	AAGTTGATAA	GGAAAAATTA	AAGGATTTTG	TTAATATGGA	TCTTGAGTTT
121	GTAAATTATA	AAGGTCCTTA	TGATTCTACA	AATACGTATG	AACAAATAGT	GGGTATTGGG
181	GAGTTTTTAG	CAAGACCGCT	GACCAATTCC	AATAGCAACT	CAAGTTATTA	TGGCAAATAT
		GATTTATTGA			GTGTTGATGT	
		CAGAGCTTGA			GAATTCTTAC	
		TCGATTATGA				TATTACAATA
421	TATAATGCTG	TTTATAGAGG	AGATTTGGAT		GGTTTTATAT	
481	TTGAAGTCTT	TAACTAAAGA	AAACGCAGGT			GTGGGCTGGA
541	AAGACTCAAA	TATTTATTCC	TCTTAAAAAG	GATATTTTGT	CTGGAAATAT	TGAATCTGAC
601	ATTGATATTG	ACAGTTTGGT	TACAGATAAG	GTGATAGCAG	CTCTTTTAAG	CGAAAATGAA
661	GCAGGCGTTA	ACTITGCAAG	AGATATTACA	GATATTCAAG	GCGAAACTCA	TAAGGCAGAT
721	CAAGATAAGA	TTGATACTGA	ATTAGACAAT	ATCCATGAAA	GCGATTCTAA	TATAACAGAA
781	ACTATTGAAA	ATTTAAGGGA	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	TAAAAAAGAG
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	.GAAAAGGAAG	AGCTAGATAA	AAAGGCAATC
901	AATCTTGATA	AAGCTCAGCA	AAAATTAGAC	TCTGCTGAAG	ATAATTTAGA	TGTTCAAAGA
961	GATACTGTTA	GAGAGAAAAT	TCAAGAGGAT	ATTAATGAGA	TTAATAAGGA	AAAGAATTTG
1021	CCAAAACCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AACTGCAAAT	AAAAGAGAGT
1081	CTAGAAGATT	TGCAGGAGCA	GCTTAAAGAA	GCTGGTGATG	AAAATCAGAA	AAGAGAAATT
1141	GAGAAGCAAA	TTGAAATCAA	AAAAAGGGAC	GAAGAACTTT	TAAAAAGTAA	AGATGGCAAA
1201	GTAAGTAAAG	ATTATGAAGC	ATTAGATCTT	GATCGAGAAT	TATCCAAAGC	TTCTAGTAAA
1261	GAAAAAAGTA	AGGTCAAGGA	AGAAGAAATA	ACTAAAGGTA	AATCACGGGC	AAGCTTAGGC
1321	GATTTGAATA	ATGATAAAA	CCTTATGTTG	CCAGAAGATC	AAAAATTACC	TGAAGATAAA
1381	AAATTGGATA	GTAAATTAGA	TGGTAAAAA	GAATTTAAAC	CAGTITCTGA	GGTTGAAAAA
		TTTCCAAGTC				
		ATGATATTGA				
		CTAAAGTTAA				
		TGTCTATAGA				
		GAACCCTGCA				
		GCATTCAGCG				
		CAGGAAAGGC				
		CTAATTITGA				
		CTGTTAGAGA				
		TGGATGAGTT				
		TATTTTAAAA		GATGAGCTTA	AAAATCTAGT	TATTTTAGAT
2101	. GTAAATACTI	TAAAAAAAGT	' TAAGTA			

K48 OSP A/ PGAU OSP A FUSION

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20 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TTT TTT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 60 70 90 TGT AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA-AAT AGC GTT TCA GTA... ACA TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTA TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 110 120 130 GAT TTA CCT GGT GGA ATG ACA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAT GGA CCA CCT TAC TGT CAA GAA CAT TCA TTT CTT TTT CTG TTT Asp Leu Pro Gly Gly Met Thr Val Leu Val Ser Lys Glu Lys Asp Lys> 160 170 180 GAC GGT AAA TAC AGT CTA GAG GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCA TTT ATG TCA GAT CTC CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Ser Leu Glu Ala Thr Val Asp Lys Leu Glu Leu Lys> 210 220 230 GGA ACT TCT GAT AAA AAC AAC GGT TCT GGA ACA CTT GAA GGT GAA ALA CCT TGA AGA CTA TTT TTG TTG CCA AGA CCT TGT GAA CTT CCA CTT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Thr Leu Glu Gly Glu Lys> 250 260 270 ACT GAC AAA AGT AAA GTA AAA TTA ACA ATT GCT GAT GAC CTA AGT CAA TGA CTG TTT TCA TTT CAT TTT AAT TGT TAA CGA CTA CTG GAT TCA GTT Thr Asp Lys Ser Lys Val Lys Leu Thr Ile Ala Asp Asp Leu Ser Gln> 300 310 320 ACT AAA TTT GAA ATT TTC AAA GAA GAT GCC AAA ACA TTA GTA TCA AAA TGA TTT AAA CTT TAA AAG TTT CTT CTA CGG TTT TGT AAT CAT AGT TTT Thr Lys Phe Glu Ile Phe Lys Glu Asp Ala Lys Thr Leu Val Ser Lys> 340 350 360 370 AAA GTA ACC CTT AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAC GAA TTT CAT TGG GAA TIT CTG TTC AGT AGT TGT CTT TTT AAG TTG CTT Lys Val Thr Leu Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

FIGURE 23 (1 of 3)

K48 OSP A/ PGAU OSPA FUSION

	390		400			410				420				430		
•	•		•		•	•		•		*	•		•		•	
														ACC		
														TGG		
Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr.	Ile	Val	Arg	Ala	Asn	Gly	Thr	yzà>	
					450			46				170			400	
	4	140		•	450		•	40	*	•	• •	* 70		•	480	
- حس ت	GAA	TAC	ACA	GAC	ATA	AAA	AGC	GAT	GGA.	TCC	GGA	AAA	GCT	AAA	GAA	
															CTT	
															Glu>	
		49	0		5	00		_	510			52	20	•		
	*		• .	*	. cm	-mm	C	CCA	3 CT	~T. 3			-	*		
														GGC		
															Lys>	
***														,		
530			540			55	50		9	60			570			
•		•	•		•		•	•		•		•	•		•	
														AAC		
														TTG		
Thr	Thr	Leu	Lys	Val	inr	GIU	GIY	INI	vai	AGI	ren	Ser	Lys	ASN	Ile>	
- 5	в̂о		. 9	590			600			61	LO		6	520		
5	80 ◆	•		590		•	600		•	61	LO .	•	6	520	•	
TTA	AAA		GGA	GAA			GTT			GAT	• GAC		GAC	ACT		
TTA TAA	AAA TTT	AGG	GGA CCT	GAA CTT	TAT	TGT	GTT CAA	CGT	GAA	GAT CTA	GAC CTG	AGA	GAC CTG	ACT TGA	TGA	
TTA TAA	AAA TTT	AGG	GGA CCT	GAA CTT	TAT	TGT	GTT CAA	CGT	GAA	GAT CTA	GAC CTG	AGA	GAC CTG	ACT TGA		
TTA TAA	AAA TTT Lys	AGG	GGA CCT	GAA CTT Glu	TAT	TGT	GTT CAA Val	CGT Ala	GAA	GAT CTA	GAC CTG Asp	AGA	GAC CTG	ACT TGA Thr	TGA Thr>	
TTA TAA	AAA TTT	AGG	GGA CCT	GAA CTT Glu	TAT	TGT	GTT CAA Val	CGT	GAA	GAT CTA	GAC CTG	AGA	GAC CTG	ACT TGA	TGA Thr>	
TTA AAT Leu	AAA TTT Lys 630	AGG Ser	GGA CCT Gly	GAA CTT Glu	TAT Ile	TGT Thr	GTT CAA Val	CGT Ala 650	GAA Leu	GAT CTA Asp	GAC CTG Asp	AGA Ser	GAC CTG Asp	ACT TGA Thr	TGA Thr>	
TTA AAT Leu CAG	AAA TTT Lys 630	AGG Ser ACT	GGA CCT Gly	GAA CTT Glu 6	TAT Ile 40 * ACT	TGT Thr • GGA	GTT CAA Val	CGT Ala 650 TGG	GAA Leu GAT	GAT CTA Asp	GAC CTG Asp 660	AGA Ser ACT	GAC CTG Asp	ACT TGA Thr	TGA Thr> 70 TTA	
TTA AAT Leu CAG	AAA TTT Lys 630 GCT CGA	AGG Ser ACT TGA	GGA CCT Gly	GAA CTT Glu 6	TAT Ile 40 + ACT TGA	TGT Thr * GGA CCT	GTT CAA Val AAA TTT	CGT Ala 650 TGG ACC	GAA Leu GAT CTA	GAT CTA Asp TCA AGT	GAC CTG Asp 660 AAA TTT	AGA Ser ACT TGA	GAC CTG Asp TCT AGA	ACT TGA Thr 67 ACT TGA	TGA Thr> 70 TTA	
TTA AAT Leu CAG	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr	GGA CCT Gly	GAA CTT Glu 6	TAT Ile 40 * ACT TGA Thr	TGT Thr * GGA CCT	GTT CAA Val AAA TTT	CGT Ala 650 TGG ACC Trp	GAA Leu GAT CTA Asp	GAT CTA Asp TCA AGT	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr	GAC CTG Asp TCT AGA	ACT TGA Thr 67 ACT TGA	TGA Thr> 70 TTA AAT Leu>	
TTA AAT Leu CAG	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA	GGA CCT Gly	GAA CTT Glu 6	TAT Ile 40 + ACT TGA	TGT Thr * GGA CCT	GTT CAA Val AAA TTT	CGT Ala 650 TGG ACC Trp	GAA Leu GAT CTA	GAT CTA Asp TCA AGT	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA	GAC CTG Asp TCT AGA	ACT TGA Thr 67 ACT TGA	TGA Thr> 70 TTA AAT	
TTA AAT Leu CAG GTC Gln	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6 AAA TTT Lys	TAT Ile 40 ACT TGA Thr 690	TGT Thr • GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp	GAA Leu GAT CTA Asp	GAT CTA Asp TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr	GAC CTG Asp * TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720	
TTA AAT Leu CAG GTC Gln	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6 AAA TTT Lys	TAT Ile 40 ACT TGA Thr 690	TGT Thr GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7	GAA Leu GAT CTA Asp	GAT CTA Asp TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr 710 GTG	GAC CTG Asp TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720	
TTA AAT Leu CAG GTC GIn	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6. AAA TTT Lys AAC TTG	TAT Ile 40 * ACT TGA Thr 690 * AGC TCG	TGT Thr GGA CCT Gly AAA TTT	GTT CAA Val AAA TTT Lys AAA TTT	CGT Ala 650 TGG ACC Trp 7 ACT TGA	GAA Leu GAT CTA Asp 00 • ACA	GAT CTA ASP TCA AGT Ser CAA GTT	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr 710 GTG CAC	GAC CTG Asp TCT AGA Ser TTT AAA	ACT TGA Thr 67 ACT TGA Thr ACT TGA	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT	
TTA AAT Leu CAG GTC GIn	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680 AGT TCA	GGA CCT Gly AAA TTT Lys GTT CAA Val	GAA CTT Glu 6. AAA TTT Lys AAC TTG	TAT Ile 40 *ACT TGA Thr 690 *AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT Lys	GTT CAA Val AAA TTT Lys AAA TTT	CGT Ala 650 TGG ACC Trp 7 ACT TGA	GAA Leu GAT CTA Asp 00 ACA TGT	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr 710 GTG CAC Val	GAC CTG Asp TCT AGA Ser TTT AAA Phe	ACT TGA Thr 67 ACT TGA Thr ACT TGA	TGA Thr> 70 TTA AAT Leu> 720 AAA	
TTA AAT Leu CAG GTC GIn	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680 AGT TCA	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6. AAA TTT Lys AAC TTG	TAT Ile 40 *ACT TGA Thr 690 *AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT	GTT CAA Val AAA TTT Lys AAA TTT	CGT Ala 650 TGG ACC Trp 7 ACT TGA	GAA Leu GAT CTA Asp 00 • ACA	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr 710 GTG CAC Val	GAC CTG Asp TCT AGA Ser TTT AAA	ACT TGA Thr 67 ACT TGA Thr ACT TGA	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT	
TTA AAT Leu * CAG GTC Gln ACA TGT	AAA TTT Lys 630 GCT CGA Ala ATT	AGG Ser ACT TGA Thr 680 AGT TCA Ser	GGA CCT Gly AAA TTT Lys GTT CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC TTG Asn	TAT Ile 40 *ACT TGA Thr 690 *AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT Lys	GTT CAA Val AAA TTT Lys AAA TTT Lys	TGG ACC Trp 7 ACT TGA Thr	GAA Leu GAT CTA ASP 00 ACA TGT Thr	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys CTT GAA Leu	AGA Ser ACT TGA Thr 710 GTG CAC Val	GAC CTG Asp TCT AGA Ser TTT AAA Phe	ACT TGA Thr 67 ACT TGA Thr ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT Lys>	
TTA AAT Leu * CAG GTC Gln ACA TGT Thr	AAA TTT Lys 630 GCT CGA Ala TAA	AGG Ser ACT TGA Thr 680 AGT TCA Ser 7	GGA CCT Gly AAA TTT Lys GTT CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC TTG Asn	TAT Ile 40 *ACT TGA Thr 690 *AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT Lys	GTT CAA Val AAA TTT Lys AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7 ACT TGA Thr	GAA Leu GAT CTA ASP 00 ACA TGT Thr	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys CTT GAA Leu	AGA Ser ACT TGA Thr 710 GTG CAC Val 7	GAC CTG ASP TCT AGA Ser TTT AAA Phe	ACT TGA Thr 67 ACT TGA Thr ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT Lys>	
TTA AAT Leu * CAG GTC Gln ACA TGT Thx	AAA TTT Lys 630 GCT CGA Ala TAA	AGG Ser ACT TGA Thr 680 AGT TCA Ser 7	GGA CCT Gly AAA TTT Lys GTT CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC TTG ASD	TAT Ile 40 * ACT TGA Thr 690 * AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT Lys 740	GTT CAA Val AAA TTT Lys AAA TTT Lys	TGG ACC Trp 7 ACT TGA Thr	GAA Leu GAT CTA Asp 00 ACA TGT Thr 750	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys CTT GAA Leu	AGA Ser ACT TGA Thr 710 GTG CAC Val 7	GAC CTG ASP TCT AGA Ser TTT AAA Phe	ACT TGA Thr 67 ACT TGA Thr TGA Thr AAT	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT Lys>	

FIGURE 23 (2 of 3)

K48 OSPA / PGAU OSP A FUSION

770 780 790 800 810

GAA GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT
CTT CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA
Glu Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asr Ala>

B20
TTA AAA TAA
AAT TTT ATT
Leu Lys ***>

FIGURE 23 (3 of 3)

B-31 OSP A /PGAU OSP A FUSION

	10				20		•	30			4	0	•		
	•		•	•		•		•	•		•		•	•	
ATG	AAA	AAA	TAT	TTA	TTG	GGA .	AŢA	GGT	CTA.	ATA	TTA	GCC	TTA	ATA	GCA
ms.c	TTT	للملحك	ልጥል	AAT	AAC	CCT	TAT	CCA	GAT	TAT	AAT	CGG	AAT	TAT	CGT
Met	Lys	Lys	Tyr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	Ile	Ala>
	-														
50			60			7	0	_		80			90		•
*		• .	•		•		~~~	- የእጥ	C	222	220	3 CC	CCT	TCA	CTA.
TGC	AAG	CAA	TAA	GTT	AGC TCG	AGC	CIT	CTA	مسد	ىلىلىك تۇمۇت	عبند	TCG	CGA	AGT	CAT
ACG	TTC	GTT	TTA	CAA	100	100	Lau	ASD	Glu	Lvs	Asn	Ser	Ala	Ser	Val>
Cys	Lys	Gin	ASI	vaı	Ser	SET.	Dea	nop		-, -					
1	00			110			120			13	30		:	140	
	•	•		*		•	•		*		•	•		•	•
GAT	TTG	CCT	GGT	GAG	ATG	AAA	GTT	CTT	GTA	AGT	AAA	GAA	AAA	GAC	AAA
ርጥክ	220	CCA	CCA	CTC	TAC	TTT	CAA	GAA	CAT	TCA	TTT	CII	LLL	CTG	TTT
Asp	Leu	Pro	Gly	Glu	Met	Lys	Val	Leu	Val	Ser	Lys	Glu	Lys	Asp	Lys>
											180			-	90
	150)		1	60		•	170		•	100		•	1.	•
*					CT 3	3 3 C	CCA	ACA	CTA	GAC	AAG	ATT	GAG	CTA	AAA
GAC	GG1	AAG	TAC	TOA:	CIA	WWG.	CGT	TGT	CAT	CTG	TTC	TAA	CTC	GAT	TTT
CTG	, CC2	. Tare	. Alc	Ser	Leu	LVS	Ala	Thr	Val	Asp	Lys	Ile	Glu	Leu	Lys>
ASP	, 613	Lys		501		, .	•••			_	-				
		200			210			2	20			230			240
•	•	•		*	•		*	•	*	*		•		•	•
GG	AC	TC	r GAI	AAA :	GAC	AAT	GGT	TCT	GGA	GTG	CTT	GAA	GGT	ACA	AAA
CCT	TG	A AG	CTA	TTI	CTG	TTA	CCA	AGA	CCI	CAC	GAA	CIT	CCA	TGT	TTT
Gly	Th	r Se	c Ası	Lys	Asp	Asn	Gly	Ser	GIA	val	ren	GIU	GIY	1 111	Lys>
			250			260			270)		2	во		
			250	•		200		*		,	•		*	•	
GA!	ת הא	C AA	A AG	באג ז	CCA	AAA	TTA	AC	ATT	GCI	'-GAC	GAT	CTA	AGT	AAA
CT	A CT	C TT	T TC	A TTT	CGI	TTT	LAA	. IGI	LAT 7	A CGA	CTG	CTA	GAT	, LCY	TTT
As	p As	p Ly	s Se	r Lys	: Ala	Lys	Lev	Thi	c Ile	e Ala	Asp	Ast	Lev	Ser	Lys>
		-													
290			30	0		3	10			320			330) - •	•
*		◆.		• 			~ ~ ` `	· ~ > '	- T CC	~ »»	N 2001	دىلەت -	י כיווי	בישרים	AGA
λC	C AC	A TT	C GA	A CI	TTA	n mana	, C44	i Cir.	7 CC	5 July 5 Yuz	ה תכי	ר אא י	CAC	AG:	TCT
TG	G TO	AA TE	G CI	TGA	A AA	1 111 1 1375	: 61:	1 As	n Gl	v Lv	s Th	r Lei	ı Va	Se	r Arg>
Tr	T TI	ir Pi	ie G1	u De	a be	. Uy.	, 01.		.						
	340			350			36	0			370			380	
	•		•	•		•		•	•		•		•		
A.	AA G	ra ac	T TO	T AG	A GA	C AA	A AC	A TC	A AC	A GA	T GA	TA A	G TT	CAA	T GAA
TO	רידי כי	ልጥ ጥር	A AC	A TC	T CT	G TT	r TG	T AG	T TG	T CT	A CT	T TA	CAA	GTT	Y C.1.1
L	s V	al Se	er Se	er Ar	g As	p Ly	s Th	r Se	r Th	r As	p Gl	u -Me	t Ph	e As	n Glux

FIGURE 24 (1 of 3)

B-31 OSP A/ PGAU OSP A FUSION

		390			4	00			110			420			4	30
	•	•		•		•	•		•		•	•		•		•
	AAA	GGT	GAA	TTG	TCT	GCA	AAA	ACC	ATG	ACA	AGA	GAA	AAT	GGA	ACC	AAA
	TTT	CCA	CTT	AAC	AGA	CGT	TIT	TGG	TAC	TGT	TCT	CTT	TTA	CCT	TGG	TIT
	Lys	Gly	Glu	Leu	Ser	Ala	Lys	Thr	Met	Thr	Arg	Glu	Asn	Gly	Thr	Lys>
	•	4	440			450			41	60			470			460
	•				•	•		•		• `	•		•		•	•
	CTT	GAA	TAT	ACA	GAA	ATG	AAA	AGC	GAT	GGA	ACC	GGA	AAA	CCI	AAA	GAA
	GAA	CTT	ATA	TGT	CTT	TAC	TTT	TCG	CTA	CCT	TGG	CCT	TTT	CGA	TIT	CII
	Leu	Glu	Tyr	Thr	Glu	Met	Lys	Ser	Asp	Gly	Thr	Gly	Lys	Ala	Lys	Glu>
			4	90			500			510			5:	20		
		•		•	•		•		•	•		•		•	•	
	GTT	ATT	AAA	AAG	TTT	ACT	CTT	GAA	GGA	AAA	GTA	GCT	AAT	GAT	AAA	GT2
	CAA	AAT	TTT	TTC	AAA	TGA	GAA	CTT	CCT	TTT	CAT	CGA	TTA	CTA	TIT	CAT
	Val	Leu	Lys	Lys	Phe	Thr	Leu	Glu	Gly	Lys	Val-	λla	Asn	Asp	ivs	Val>
			_	•		•			_					_	-,, -	
	530		_	540		_	5:	50	_	:	560			570		
				· C		~	œ.	``		٠			•	•		•
	ACA	116	GAA	GIA	AAA	CMM	COM	ACC	GTT	ACT	TTA	AGT	AAG	GAA	ATT	GCA
	2 G 1	AAC	CII	UAT	111	CII	CCT	766	CAA	TGA	AAT	TCA	TIC	CTT	TAA	CCI
	inr	reu	GIU	Val	Lys	GIU	GIY	Thr	vai	THE	Leu	Ser	Lys	Glu	Ile	Ala>
	- 58	30		5	90			600			- 61	.0		6	520	
					•					•		•	•		•	
	AAA	TCT	GGA	GAA	GTA	ACA	GTT	GCT	CTT	AAT	GAC	ACT,	AAC	ACT	ACT	CAG
	TTT	AGA	CCT	CTT	CAT	TGT	CAA	CGA	GAA	TTA	CTG	TGA	TTG	TGA	TGA	GTC
	Lys	Ser	GIA	Glu	Val	Thr	Val	Ala	Leu .	Asn	Asp	Thr	Asn	Thr	Thr	Gln>
		630			64	0	•	-							67	0
	•	•							550			660				
				•		•	•		•		•	•		•		•
	GCT	ACT	AAA	AAA	ACT	• GGC	• GCA	TGG	• GAT	TCA	+ AAA	* ACT	TCT	ACT	TTA	ACA
	CGA	TGA	TTT	TTT	TGÀ	CCG	CGT	TGG	GAT CTA	AGT	TTT	ACT TGA	AGA	TGA	ATT AAT	ACA TGT
*	CGA	TGA	TTT	TTT	TGÀ	CCG	CGT	TGG	GAT CTA	AGT	TTT	ACT TGA	AGA	TGA	TTA	ACA TGT
	CGA	TGA Thr	TTT Lys	TTT	TGÀ	CCG Gly	CGT	TGG	GAT CTA Asp	AGT	TTT	ACT TGA Thr	AGA Ser	TGA	ATT AAT	ACA TGT Thr>
*	CGA	TGA Thr	TTT	TTT	TGÀ	CCG	CGT	TGG	GAT CTA	AGT	TTT	ACT TGA Thr	AGA	TGA	ATT AAT	ACA TGT
*	CGA Ala	TGA Thr	TTTT	TTT Lys	TGA Thr	Gly 690	CGT Ala	TGG ÄCC Trp	GAT CTA Asp	AGT Ser	TTT Lys	ACT TGA Thr	AGA Ser	TGA Thr	TTA AAT Leu	ACA TGT Thr>
*	CGA Ala •	TGA Thr	TTT Lys 80 GTT	TTT Lys AAC	TGA Thr • AGC	CCG Gly 690 AAA	CGT Ala	TGG ACC Trp	GAT CTA Asp 70	AGT Ser 00 • CAA	TTT Lys -	ACT TGA Thr 7	AGA Ser 10	TGA Thr ACT	TTA AAT Leu AAA	ACA TGT Thr>
	CGA Ala ATT TAA	TGA Thr AGT TCA	TTT Lys 80 GTT CAA	TTT Lys AAC TTG	TGA Thr • AGC TCG	CCG Gly 690 • AAA TTT	CGT Ala	TGG ACC Trp ACT TGA	GAT CTA Asp 70 ACA TGT	AGT Ser 00 • CAA GTT	TTT Lys CTT GAA	ACT TGA Thr Thr GTG CAC	AGA Ser 10 TTT	TGA Thr ACT TGA	TTA AAT Leu AAA TTT	ACA TGT Thr>
*	CGA Ala ATT TAA	TGA Thr AGT TCA	Lys 580 GTT CAA Val	Lys AAC TTG Asn	TGA Thr • AGC TCG	CCG Gly 690 * AAA TTT Lys	AAA TTT Lys	TGG ACC Trp ACT TGA	GAT CTA Asp 70 ACA TGT	AGT Ser 00 • CAA GTT Gln	TTT Lys CTT GAA	ACT TGA Thr Thr GTG CAC	AGA Ser 10 TTT AAA Phe	TGA Thr ACT TGA Thr	TTA AAT Leu AAA TTT	ACA TGT Thr> 720 CAA GTT
*	CGA Ala ATT TAA	TGA Thr AGT TCA	TTT Lys 80 GTT CAA	Lys AAC TTG Asn	TGA Thr • AGC TCG	CCG Gly 690 * AAA TTT Lys	CGT Ala	TGG ACC Trp ACT TGA	GAT CTA Asp 70 ACA TGT	AGT Ser 00 • CAA GTT	TTT Lys CTT GAA	ACT TGA Thr Thr GTG CAC	AGA Ser 10 TTT	TGA Thr ACT TGA Thr	TTA AAT Leu AAA TTT	ACA TGT Thr> 720 CAA GTT
	CGA Ala ATT TAA Ile	TGA Thr AGT TCA Ser	TTT Lys 580 GTT CAA Val	AAC TTG Asn	TGA Thr AGC TCG Ser	CCG Gly 690 AAA TTT Lys	AAA TTT Lys	TGG ACC Trp • ACT TGA Thr	GAT CTA ASP 70 ACA TGT Thr	AGT Ser CAA GTT Gln 750	TTT Lys CTT GAA Leu	ACT TGA Thr 7 GTG CAC Val	AGA Ser 10 TTT AAA Phe	TGA Thr ACT TGA Thr	TTA AAT Leu AAA TTT Lys	ACA TGT Thr> 720 CAA GTT Gln>
	CGA Ala ATT TAA Ile	TGA Thr AGT TCA Ser	TTT Lys 580 GTT CAA Val 73	AAC TTG ASD ACT	TGA Thr AGC TCG Ser	CCG Gly 690 AAA TTT Lys	AAA TTT Lys	TGG ACC Trp ACT TGA Thr	GAT CTA ASP 70 ACA TGT Thr	AGT Ser OO CAA GTT Gln 750	TTT Lys CTT GAA Leu	ACT TGA Thr GTG CAC Val	AGA Ser 10 TTT AAA Phe 76	TGA Thr ACT TGA Thr	TTA AAT Leu AAA TTT	ACA TGT Thr> 720 CAA GTT Gln>

FIGURE 24 (2 of 3)

B-31 OSP A /PGAU OSP A FUSION

770 780 790 800 810

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA

CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT

Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys ***

FIGURE 24 (3 of 3)

B31/K48 fusion

10 20 40 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 50 60 70 . 80 TGT AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA AAC AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTG CTC TTT TTG TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 100 110 120 140 GAT TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA CTA AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT Asp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asn Lys> 150 160 170 180 GAC GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Asp Leu Ile Ala Thr Val Asp Lys Leu Glu Leu Lys> 200 210 220 230 GGA ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA CCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Val Leu Glu Gly Val Lys> 250 260 270 . GCT GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA CGA CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT Ala Asp Lys Ser Lys Val Lys Leu Thr Ile Ser Asp Asp Leu Gly Gln> 290 300 310 320 330 ACC ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA TGG TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT Thr Thr Leu Glu Val Phe Lys Glu Asp Gly Lys Thr Leu Val Ser Lys> 340 350 360 370 380 AAA GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA TIT CAT TGA AGG TIT CTG TTC AGT AGT TGT CIT TIT AAG TTA CIT Lys Val Thr Ser Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu> 390 400 410 420 430 AAA GGT GAA GTA TCT GAA AAA ATA ATA ACA AGA GCA GAC GGA ACC AGA TIT CCA CTT CAT AGA CTT TTT TAT TAT TGT TCT CGT CTG CCT TGG TCT Lys Gly Glu Val Ser Glu Lys Ile Ile Thr Arg Ala Asp Gly Thr Arg> FIGURE 25 (1 of 2)

B31/K48 fusion

450 470 CTT GAA TAC ACA GGA ATT AAA AGC GAT GGA TCT GGA AAA GCT AAA GAG GAA CTT ATG TGT CCT TAA TTT TCG CTA CCT AGA CCT TTT CGA TTT CTC Leu Glu Tyr Thr Gly Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 500 510 520 GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA CAA AAT TIT CCG ATA CAA GAA CIT CCT TGA GAT TGA CGA CIT TIT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr> = := : 560 570 530 ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser> 590 600 610 AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala> 630 640 650 660 GCT ACT AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA CGA TGA TTT TTT TGA CGT CGA ACC TTA AGT TTT TGA AGG TGA AAT TGT Ala Thr Lys Lys Thr Ala Ala Trp Asn Ser Lys Thr Ser Thr Leu Thr> 690 680 700 710 720 ATT AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC AGA AAA GAA TAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT Ile Ser Val Asn Ser Gln Lys Thr Lys Asn Leu Val Phe Thr Lys Glu> 730 740 750 760 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA GAA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT CTT Asp Thr Ile Thr Val Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu Glu> 780 800 770 810 GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys ***>

FIGURE 25 (2 of 2)

B-31 OSP A/ 25015 OSP A FUSION

															•
	_		10	_		20			31	0			40	-	
እጥ	- 338				mmo	*		•		•	•		•	•	•
71C	ን ሌሌላ ጉጥጥ	, 47474 1	LAT	דע ג	716	CCT	ATA		CTY	ATA	TTA	GCC	TT	ATA	GCA
Met	Lvs	Lvs	תנת דער	Leu	Leu	Gly	The	610	LOA	TAL	TAN	CGG	AAT	TAT	CGT Ala>
		-, -	-1-	202		013		. Gly	Det		Leu	MIS	ren	ile	Ala>
50			60				70			80			90		•
. •		•	•		•		•	•		•		•	•		•
TGI	` AAG	CAA	AAT	GTT	AGC	AGC	CTI	GAC	GAG	AAA	AAC	AGC	GII	TCA	GTA
ACA	1110	GIT	TTA	CAA	TCG	TCG	GAA	CTG	CTC	TIT	TIG	TCG	CAA	AGT	CAT
Cys	Lys	GIN	ASD	vai	ser	Ser	Leu	Asp	GIU	L <u>y</u> s	.Asn	Ser	Val	Ser	Val>
1	00			110			120	•		7	30			1/0	
	•	•		•		•	•		*		•	•		140	
GAT	TIG	CCT	GGT	GAA	ATG	AAA	GTT	CIT	GTA	AGC	AAA	GAA	AAA	AAC	AAA
CTA	AAC	GGA	CCA	CTT	TAC	TTT	CAA	GAA	CAT	TCG	TTT	CTT	للملمك	TTC	, Julius
Asp	Leu	Pro	Gly	Glu	Met	Lys	Val	Leu	Val	Ser	Lys	Glu	Lys	Asn	Lys>
	150			1 (60			170			180				
•	•		•	-	*	•		•		•	100			1:	90
GAC	GGC	AAG	TAC	GAT	CTA	ATT	GCA	ACA	GTA	GAC	AAG	CTT	GAG	لىت.	444
CTG	CCG	TTC	ATG	CTA	GAT	TAA	CGT	TGT	CAT	CTG	TTC	GAA	CTC	CAA	للملحك
Asp	Gly	Lys	Tyr	Asp	Leu	Ile	Ala	Thr.	Val	Asp	Lys	Leu	Glu	Leu	Lys>
	•	200			210			2.	20						
	•	*		•	*		•	۷.	*	•	•	230			240
GGA	ACT	TCT	GAT	AAA	AAC	AAT	GGA	TCT	GGA	GTA	CTT	GAA	ccc	GTA	222
CCT	TGA	AGA	CTA	TTT	TTG	TTA	CCT	AGA	CCT	CAT	GAA	CTT	CCG	CAT	ململمك
Gly	Thr	Ser	Asp	Lys	Asn	Asn	Gly	Ser	Gly	Val	Leu	Glu	Gly	Val	Lys>
		25	50		-	60			270				_		
	•		•	•	-	*		•	270		•	28	•		
GCT	GAC	AAA	AGT	AAA	GTA	AAA	ATT	ACA	ATT	TCT	GAC	GAT	CTA	GGT	CAA
CGA	CTG	TTT	TCA	TTT	CAT	TTT	AAT	TGT	TAA	AGA	CTG	CTA	CAT	CCA	CTT
Ala	ХSР	Lys	Ser	Lys	Val	Lys	Leu	Thr	Ile	Ser	Asp	Asp	Leu	Gly	Gln>
290			300			31	0		••	20					
•		•	*	•	•			•	-	\$20		•	330		•
ACC	ACA	CTT	GAA	GTT	TTC	AAA	GAA	GAT	GGC	AAA	ACA	CTA ·	СТА	4 0T	444
166	101	GAA	CTT	CAA	AAG	TIT	CII	CTA.	CCG	TTT	TGT	CAT	ChT	ACT	لملحك
Thr	Thr	Leu	Glu	Val	Phe	Lys	Glu	Asp	Gly	Lys	Thr	Leu	Val	Ser	Lys>
. 34	10			50			3.00				_				
	•	•	د	•		•	360		•	37	•	•	3	80	
AAA	GTA	ACT	TCC	AAA	GAC	AAG	TCA	TCA	ACA	GAA	GAA	444	TT C	- 22T	C A A
$ ext{TTT}$	CAT	TGA	AGG	TTT	CTG	TTC	AGT	AGT	TGT	CTT	CTT	طملمك	226	מדד	-1-1-
Lys	Val	Thr	Ser	Lys	Asp	Lys	Ser	Ser	Thr	Glu	Glu	Lys	Phe	Asn	Glu>

FIGURE 26 (1 of 3)

B-31 OSP A/ 25015 OSP A FUSION

	390			4(00			410			420			4	30
•	•		•		•	•		*		•	•		•		•
															AGA
TTT	CCA	CTT	CAT	AGA	CIT	TIT	TAT	TAT	TGT	TCT	CGT	CIG	CCT	TGG	TCT
Lys	GIY	GIU	vaı	ser	GIU	Lys	TTE	lle	Thr	Arg	Ala	Asp	Gly	Thr	Arg>
	4	140			450			. 4	60			470			480
•		•		•	•		•	-	•	•		•		•	+
CTT	GAA	TAC	ACA	GGA	ATT	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCT	AAA	GAG
GAA	CII	ATG	TGT	CCT	TAA	TTT	TCG	CTA	CCT	AGA	CCT	TTT	CGA	TIT	CTC
Leu	Glu	Tyr	Thr	Gly	Ile	Lys	Ser	Asp	CJA	Ser	Gly	Lys	Ala	Lys	Glu>
		49	90		9	500			510			5:	20		
	•		•	•		•		•	•		•		*	•	
GTT	TTA	AAA	GGC	TAT	GTT	CTT	GAA	GGA	ACT	CTA	ACT	GCT	GAA	AAA	ACA
CAA	AAT	TTT	CCG	ATA	CAA	GAA	CTT	CCT	TGA	GAT	TGA	CGA	CTT	TTT	TGT
vai	ren	Lys	GIĀ	TYT	Vai	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys	Thr>
530			540			5	50		9	560			570		
•		•	*		*		*	•		•		•	•		•
ACA	TTG	GTG	GTT	AAA	GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	TTA	TCA
TGT	AAC	CAC	CAA	TTT	CTT	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	TAA	AGT
1111	Den	V & 1	Val	Lys	GIU	GIÀ	Int	vaı	Inr	ren	Ser	Lys	Asn	Ile	Ser>
58	30		5	590			600			61	.0		•	520	
	•	•		•		•	•		•		•	•		•	
AAA	• TCT	GGG	GAA	GTT	TCA	GTT	GAA	CTT	AAT	GAC	• ACT	GAC	AGT	AGT	GCT
AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TTT	TCT AGA Ser	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	GCT CGA Ala>
AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA Ala>
AAA TTT Lys	TCT AGA Ser 630	Gly	GAA CTT Glu	GTT CAA Val	AGT Ser	CAA Val	GAA CTT Glu	GAA Leu 550	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
AAA TTT Lys GCT	TCT AGA Ser 630	CCC Gly AAA	GAA CTT Glu	GTT CAA Val 64	AGT Ser 10 • GCA	CAA Val	GAA CTT Glu	GAA Leu 550	TTA Asn GCA	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala>
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 AAT TTA	TTA Asn GCA CGT	GAC CTG Asp	ACT TGA Thr 660 ACT TGA	CTG Asp TCA AGT	AGT TCA Ser • ACT	AGT TCA Ser 67 TTA AAT	CGA Ala> C ACA TGT
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 GCA CGT Ala	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 AAT TTA Asn	TTA Asn GCA CGT Ala	GAC CTG Asp	ACT TGA Thr 660 ACT TGA	CTG Asp TCA AGT	AGT TCA Ser • ACT	AGT TCA Ser 67 TTA AAT	CGA Ala>
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 AAT TTA	TTA Asn GCA CGT Ala	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCA AGT	AGT TCA Ser • ACT	AGT TCA Ser 67 TTA AAT	CGA Ala> C ACA TGT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 10 GCA CGT Ala 690	CAA Val • GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA Asn	TTA Asn GCA CGT Ala	GAC CTG Asp • GGC CCG Gly	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCA AGT Ser	AGT TCA Ser • ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> C ACA TGT Thr> 720
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 580 •	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 10 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC TIP	GAA Leu 550 AAT TTA ASD 70	GCA CGT Ala	GAC CTG Asp * GGC CCG Gly	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> C ACA TGT Thr> 720 CAA
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys 580 GTA	GAA CTT Glu AAA TTT Lys AAC TTG	GTT CAA Val 64 ACT TGA Thr AAC TTG	AGT Ser 10 GCA CGT Ala 690 AAA TTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC TIP	GAA Leu 550 AAT TTA ASD 70	GCA CGT Ala	GAC CTG Asp 	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser 710	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> C ACA TGT Thr> 720 CAA
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 80 GTA CAT Val	GAA CTT Glu AAA TTT Lys AAC TTG ASN	GTT CAA Val 64 ACT TGA Thr AAC TTG	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC TIP	GAA Leu 550 AAT TTA ASD 70	GCA CGT Ala O GCC CGG Ala	GAC CTG Asp 	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser 710 TTT AAA Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> C ACA TGT Thr> 720 CAA GTT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 80 GTA CAT Val	GAA CTT Glu AAA TTT Lys AAC TTG	GTT CAA Val 64 ACT TGA Thr AAC TTG	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC TIP	GAA Leu 550 AAT TTA ASD 70	GCA CGT Ala	GAC CTG Asp 	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser 710	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> C ACA TGT Thr> 720 CAA GTT
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr ACT TGA Thr	CCC Gly AAA TTT Lys 580 GTA CAT Val	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG Asn	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys	GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASD 70 AAA TTT Lys	GCA CGT Ala OCC CGG Ala 750	GAC CTG Asp GGC CCG Gly CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 710 TTT AAA Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> CO ACA TGT Thr> CAA GTT Gln>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr ACT TGA Thr	CCC Gly AAA TTT Lys 580 GTA CAT Val 7:	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG Asn TCA AGT	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys CAA GTT	CAA Val GCT CGA Ala AAA TTT Lys AAA TTT	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASD 70 AAA TTT Lys	GCA CGT Ala OCC CGG Ala 750 TCA AGT	GAC CTG Asp GGC CCG Gly CTT GAA Leu GCA CGT	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 710 * TTT AAA Phe 76	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys TTG AAC	CGA Ala> CCAA TGT Thr> CAA GTT Gln> GAA CTT
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr ACT TGA Thr	CCC Gly AAA TTT Lys 580 GTA CAT Val 7:	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG Asn TCA AGT	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys CAA GTT	CAA Val GCT CGA Ala AAA TTT Lys AAA TTT	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASD 70 AAA TTT Lys	GCA CGT Ala OCC CGG Ala 750 TCA AGT	GAC CTG Asp GGC CCG Gly CTT GAA Leu GCA CGT	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 710 * TTT AAA Phe 76	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys TTG AAC	CGA Ala> CO ACA TGT Thr> CAA GTT Gln>

FIGURE 26 (2 of 3)

49//33

B-31 OSP A/ 25015 OSP A FUSION

770			780			79	90		1	800			810		
•		•			•		•	•		•		•	•		•
CCG	TGT	CGT	CAG	CTT	ATT TAA Ile	TTT	TGT	GAA	CTA	CTT	GAA	TTT	TTG	CGA	

AGA TCT Arg>

FIGURE 26 (3 of 3)

K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

10	20)	30	40	
* *	•	•	• •	• •	
ATG AAA AAA TAT	TTA TTG G	GA ATA GGT	CTA ATA TTA	GCC TTA ATA	GCA
TAC TTT TTT ATA	AAT AAC CO	CT TAT CCA	GAT TAT AAT	CGG AAT TAT	CGT
Met Lys Lys Tyr	Leu Leu G	ly Ile Gly	Leu Ile Leu	Ala Leu Ile	Ala>
50 60	1	70	80	90	•
TGT AAG CAA AAT		CC CTT C	CAN ANN ANT	ACC CTT TCA	GTA .
TGT AAG CAA AAT ACA TTC GTT TT	CAN TOO TO	CC CAA CTA	CUT TITE TIL	TCC CAA ACT	CAT
Cys Lys Gln Ass	CAA 1CG 1	CG GWY CIN	Glu Ive Asn	Ser Val Ser	Val.
CAS TAS CIU MEI	1 val ser s	et pen wab			1427
100	110	120	130	140	
• •	•	•	* *	•	
GAT TTA CCT GGT	GGA ATG A	CA GTT CTT	GTA AGT AAA	GAA AAA GAC	AAA
CTA AAT GGA CCA	CCT TAC T	GT CAA GAA	CAT TCA TTT	CTT TTT CTG	TTT
Asp Leu Pro Gly	Gly Met T	hr Val Leu	Val Ser Lys	Glu Lys Asp	Lys>
	1.60	170	180	1	90
150	160	170	700	• •	•
GAC GGT AAA TA	י האכיד רידא כי	NG GCA ACA	GTA GAC AAG	CTT GAG CTT	AAA
CTG CCA TTT AT	TCA GAT C	TC CGT TGT	CAT CTG TTC	GAA CTC GAA	TTT
Asp Gly Lys Ty	r Ser Leu G	lu Ala Thr	Val Asp Lys	Leu Glu Leu	Lys>
Map Gij bjo ij		<u> </u>			_
200	210	22	20 2	230	240
• •	• •	•	*	•	•
GGA ACT TCT GA	AAA AAC A	AAC GGT TCT	GGA ACA CTT	GAA GGT GAA	AAA
CCT TGA AGA CT	A TTT TIG I	TTG CCA AGA	CCT TGT GAA	CIT CCA CIT	1-1-1
Gly Thr Ser As	p Lys Asn A	Asn Gly Ser	GIY Thr Leu	Gin Giv Gin	: Lys>
250	26	50	270	280	
. •	•	•	•	* *	
ACT GAC AAA AG	T AAA GTA A	AAA TTA ACA	ATT GCT GAT	GAC CTA AGI	CAA
TGA CTG TTT TO	A TIT CAT 7	TTT AAT TGT	TAA CGA CTA	CTG GAT TCA	GTT
Thr Asp Lys Se	r Lys Val I	Lys Leu Thr	Ile Ala Asp	Asp Leu Ser	Gln>
290 30	0	310	320	330	
	• •	• •	•	• •	•
1,01 100 100			GCC AAA ACA		
TGA TTT AAA CT	T TAA AAG 1	TTT CTT CTA	CGG TTT TGT	AAT CAT AG	r TTT
Thr Lys Phe G	u Ile Phe	Lys Glu Asp	Ala Lys Thr	Leu Val Se	r Lys>
340	350	360	370	380	
* *	•	* *	•	• •	
AAA GTA ACC.C	T AAA GAC	AAG TCA TCA	ACA GAA GAA	AAA TTC AA	C GAA
TTT CAT TGG G	AA TTT CTG	TTC AGT AGT	TGT CTT CTT	TIT AAG II	G CTT
Lys Val Thr L	eu Lys Asp	Lys Ser Ser	Thr Glu Glu	Lys Phe As	n Glu>

FIGURE 27 (1 of 3)

K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

		390			40	0	•	.4	10		•	420		•	43	0
	\ \ \	CCT	GAA	בטע	тст	CYY	AAA	ACA	ATA	GTA	AGA	GCA	TAA	GGA	ACC	AGA
	TTC	CCA	CTT	TGT	AGA	CTT	TTI	TGT	TAT	CAT	TCT	CGT	ATT	CCT	TGG	TCT
	LVS	Glv	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
	<i>D</i> , <i>D</i>					450	-		46				70			480
	•	•	140		•	*		•		•	•		•		•	•
	СТТ	GAA	TAC	ACA	GAC	ATA	AAA	AGC	GAT	GGA	TCC	GGA	AAA	GCT	AAA	GAA
	GAA	CTT	ATG	TGT	CTG	TAT	TTT	TCG.	CTA	CCT	AGG.	CCT	TTT	CGA	TTT	CII
	Leu	Glu	Tyr	Thr	Asp	Ile	Lys	Ser	Asp	Gly	Ser	Cly	Lys	Ala	Lys	Glu>
			49) n		5	00			510			52			
		•	7.	•	•	_	•		•	•		•		•	•	
-	GTT	TTA	AAA	GAC	TTT	ACT	CTT	GAA	GGλ	ACT	CTA	GCT	GCT	GAC	GGC	AAA
	CAA	AAT	TTT	CTG	AAA	TGA	GAA	CTT	CCT	TGA	GAT	CGA	CGA	CTG	CCG	TTT
	Val	Leu	Lys	Asp	Phe	Thr	Leu	Glu	Gly	Thr	Leu	Ala	Ala	Asp	Gly	Lys>
	530			540			55	0		9	560			570		
	•		•	•		•		•	•		•		• .	•		•
	ACA	ACA	TTG	AAA	GTT	ACA	GAA	GGC	ACT	GTT	GTT	TTA	AGC	AAG	ATT	TCA
j.	TGT	TGT	AAC	TTT	CAA	TGT	CTT	CCG	TGA	CAA	CAA	AAT	TCG	TTC	TAA	AGT
	Thr	Thr	Leu	Lys	Val	Thr	Glu	Gly	Thr	Val	vai	Leu	Ser	rys	TIE	Ser>
	5	80			590		_	600		_	63	10		•	520	
·±		•	•		•	TCA	•	•	رست	• •		. •	•		•	GC7
·	AAA	• TCT	GGG	GAA	GTT	TCA	GTT	• GAA	CTT	AAT	GAC	.+ ACT	GAC CTG	AGT	• AGT	GCT CGA
	AAA TTT	TCT	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGY
-4- 	AAA TTT	TCT	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	GCT CGA Ala>
-2-	AAA TTT	TCT	CCC Gly	GAA CTT	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA Ser	CGY
	AAA TTT Lys	TCT AGA Ser	CCC	GAA CTT Glu	GTT CAA Val	AGT Ser 40	CAA Val	GAA CTT Glu	GAA Leu 50	TTA Asn	GAC CTG Asp	ACT TGA Thr	Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
-2-	AAA TTT Lys	TCT AGA Ser 630	CCC Gly	GAA CTT Glu	GTT CAA Val 6	AGT Ser 40 •	CAA Val	GAA CTT Glu	GAA Leu 550 AAT	TTA ASD TCA	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala> 70 • ACA
	AAA TTT Lys GCT	TCT AGA Ser 630	CCC Gly AAA	GAA CTT Glu AAA	GTT CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 50 AAT TTA	TTA ASD TCA AGT	GAC CTG Asp * AAA TTT	ACT TGA Thr 660 ACT TGA	CTG Asp TCC AGG	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 ACA TGT
	AAA TTT Lys GCT	TCT AGA Ser 630	CCC Gly AAA	GAA CTT Glu AAA	GTT CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 50 AAT TTA	TTA ASD TCA AGT	GAC CTG Asp * AAA TTT	ACT TGA Thr 660 ACT TGA	CTG Asp TCC AGG	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 • ACA
	AAA TTT Lys GCT	TCT AGA Ser 630	CCC Gly AAA	GAA CTT Glu AAA	GTT CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 50 AAT TTA Asn	TTA ASD TCA AGT	GAC CTG Asp * AAA TTT	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCC AGG	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 ACA TGT
	AAA TTT Lys GCT	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT Lys	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA Asn	TTA ASD TCA AGT Ser	GAC CTG ASP * AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser * ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr>
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACI TGA Thr	CCC Gly AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA Asn 7	TTA ASD TCA AGT Ser	GAC CTG Asp * AAA TIT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 CAA	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA ASD 7	TTA ASD TCA AGT Ser 00 AAC	GAC CTG Asp AAA TIT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 CAA	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA ASD 7	TTA ASD TCA AGT Ser 00 AAC	GAC CTG Asp AAA TIT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 CGTG CAC	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 550 AAT TTA ASD 7	TTA ASD TCA AGT Ser 00 AAC	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT
	AAA TTT Lys GCT CGA Ala ATI TAA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA AST	GTT CAA Val 6 ACT TGA Thr AGC TCG Ser	AGT Ser 40 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACC TGG	GAA Leu 550 AAT TTA ASN 7 AAA TTT Lys	TTA ASD TCA AGT Ser OO AAC TTG ASD	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser 710 TTC AAG Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>
	AAA TTT Lys GCT CGA Ala ATI TAA	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser	CCC Gly AAA TTT Lys 680 CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA AST	GTT CAA Val 6 ACT TGA Thr AGC TCG Ser	AGT Ser 40 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 550 AAT TTA ASD 7 AAA TTT Lys	TTA ASD TCA AGT Ser 00 AAC TTG ASD	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>
	AAA TTT Lys GCT CGA Ala ATI TAM	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACT TCA TCA TTCA TTCA TTCA TTCA TTCA T	CCC Gly AAA TTT Lys 680 CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA AST	GTT CAA Val 6 ACT TGA Thr AGC TCG Ser	AGT Ser 40 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 550 AAT TTA ASD 7 AAA TTT Lys	TTA ASD TCA AGT Ser 00 AAC TTG ASD 750 TCA	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe TTC AAG	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys CTA GAT	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>

FIGURE 27 (2 of 3)

K48 OSP A / B-31 OSP A/ K48 OSP A FUSION

770 780 790 800 810

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA
CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT
Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys ***>

FIGURE 27 (3 of 3)

B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

		_		3	10			20			3	0			40		
	እ ጥ(- 22	x x	7. 7.	T 3 4	, ,	• •	•		•		•	•	•	•		•
	TAC	3 AA	ው ጥ የ	Դ	ንጥ ነ	1 1 2 7 7 A A A	r 231	- 667	L AT	A GG	T CT	'A AT	'A TT	A GC	CIT	A AT	A GCA T CGT
	Met	Ly	s L	ys	Tyr	Lei	Lei	GIV	. IN.	- Cl	M GM G.T. V	1 1A	T AA	r CG	S AA	T TA	T CGT e Ala:
		•		•		:		,		- 01	, De	u II	e Le	n WIS	a Le	u II	e Ala:
	50				60				70			80			9	D	
	•		•		•		•		•	. •	• .	•		•			•
	TGT	C AA	G C	AA	AAT	GTT	, AGC	AGC	CI	CA:	r ga	AA A	A AA:	r Ago	GT	r TC	A GTA
	~~~		. ب	T T	TIM		1 1700	100	GAA	CT	CT	T TI	ניתים ית	1 TYCE	- CA	~	
	٠, ١	. <b>.</b>			veri	451	. <i>J</i> e1	Ser	rec	ASĮ	5 G11	u Ly	s Asi	n Ser	Va.	l Se	r CAT
	1	.00				110			120	· )			130			140	
		•		•		•		•		•	•		•	•	,	140	
	GAT	TT	C	CT	GGT	GGA	ATG	ACA	GTT	CII	GT	A AG	AAA 1	GAA	AA	GAC	AAA :
	CIN	~~~	. G	3 M	CLA	CCI	TAC	TGT	CAA	GAA	CAT	ו דר	T TOTAL	, C-T	•		
	vah	Let	1 2	О	CIÀ	GIĀ	met	Thr	Val	Leu	Val	l Se	Lys	Glu	Lys	Asp	TIT Lys>
		150	)			1	60			170			180			_	
	• ,		•		•		•	•		•	•	•	•		•		.90
	GAC	GGT	, Y1	A	TAC	AGT	CTA	GAG	GCA	ACA	GT2	GAC	: AAG	CTT	GAG	CTT	AAA
	C10				AIG	TCA	GAT	CTC	CGT	TGT	CAT	` ሮሞር	المناس :	C 2 2	~~~		
	ASP	GIY	T-3	/5	ıyr	Ser	Leu	Glu	Ala	Thr	Val	Asp	Lys	Leu	Glu	Leu	Lys>
			200	)			210			2	20			220			
	÷		•			•			•		•	•		230			240
	GGA	ACT	TC	T	GAT	AAA	AAC	AAC	GGT	TCT	GGA	ACA	CTT	GAA	GGT	GAA	444
		IGA	AC	, A	CTA	J-J-I.	TTG	TTG	CCA	AGA	CCT	TGT	CAA	شش	CCN	~~~	
	GIĀ	inr	56	r	Asp	Lys	Asn	Asn	Gly	Ser	Gly	Thr	Leu	Glu	Gly	Glu	Lys>
				25	0		2	260			270			~	· ·		
		•			•	•		•		•	*		•	2.8			
	ACT	GAC	AA	Α.	AGT	AAA	GTA	AAA	TTA	ACA	ATT	GCT	GAT	GAC	CTA	AGT	CAA
	1 G.	C10	- 4 4	4	ICA	111	CAT	1-1-1.	AAT	TGT	ጥልል	CCA	CTX	CTC	0 3 m		
	inr	ASP	Ly	5	ser	Lys	Val	Lys	Leu	Thr	Ile	Ala	Asp	Asp	Leu	Ser	GTT Gln>
2	90			:	300			31	0			320			220		
	•		•		*		•		•	•		•		•	330		•
	ACT	AAA	TT	T	GAA	ATT	TTC	AAA	GAA	GAT	GCC	AAA	ACA	TTA	GTA	TCA	AAA
	TOA	J-1-1.	AA	A (	CIT	TAA	AAG	TTT	CTT	CTA	CGG	delet.	TV-T	AAT	CAT	AGT	TTT
	1111	Lys	Pn	е (	3111	lle	Phe	Lys	Glu	Asp	Ala	Lys	Thr	Leu	Val	Ser	TTT Lys>
	34	10			3	50			360			. ,	7.0		_	<u>.</u> .	
		•		*		•		•	•		•		70 *	•		80	
	AAA	GTA	AC	C	CTT	AAA	GAC	AAG	TCA	TCA	ACA	GAA	GAA	AAA	TTC	ם ב	643
	4, 4, 4	~~v *		y (	3MM	111	CIG	TTC	AGT	ACT	TCT		CAAL	TWO THE			
	rys	val	Th	r I	Len	Lys	Asp	Lys	Ser	Ser	Thr	Glu	Glu	Lys	Phe	Asn	CIT Glu>

FIGURE 28 (1 of 3)

# 54/133 B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

	390			40	00			410			420			4	30 .
. • .	•		•		•	•		. •	•	•	•		•		•
										AGA					
										TCT					
Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
	4	140		•	450.		•	- 41	50	•	4	170		_	480
بلمك	440	TAC	ACA	GAC	•	222	ACC.	GAT	CCA	TCC	GGA	444	COT	222	CN
										AGG					
Leu	Glu	Tyr	Thr	Asp	Ile	Lys	Ser	Asp	Gly	sēr'	Gly	Lvs	Ala	Lvs	Glu>
		•		•				•						-,-	010>
		49	90		5	500	•		510			52	20		
	•		•	*		•		•	•		•		•	•	
										CTA					
										GAT					
Val	Leu	Lys	Asp	Pne	Thr	Leu	GIA	GIA	Thr	Leu	Ala	Ala	Asp	Gly	Lys>
530			540			5	50			560			570		
•	•	•	•		•	-	•	•		•		•	J. 0		•
ACA	ACA	TTG	AAA	GTT	ACA	GAA	GGC	ACT	GTT	GTT	TTA	AGC	AAG	ATT	TCA
										CAA					
Thr	Thr	Leu	Lys	Val	Thr	Glu	Gly	Thr	Val	Val	Leu	Ser	Lys	Ile	Ser>
-		•							÷·		_				
31	30 •	*	:	90			600			61	.0		€	20	
AAA	TCT	GGG	GAA	GTT	TCA	GTT	GAA	77	AAT	GAC	- УСТ	GAC.	ACT	»CT	CCT
										CTG					
															Ala>
										_		-			
	630			64	10		6	550			660			67	0
•	•		•		•	•		*		•	•		•		•
										AAA					
										TTT					
776	1111	Ly S	Lys	1111	MIG	WIG	пр	ASII	Ser	Lys	lnr	Ser	Thr	Leu	Thr>
	(	680			690			70	00		7	710			720
•		•		•	•		•		•	•	-	•		•	•
ATT	AGT	GTG	AAT	AGC	CAA	AAA	ACC	AAA	AAC	CTT	GTA	TTC	ACA	AAA	GAA
AAT	TCA	CAC	TTA	TCG	GTT	TTT	TGG	TTT	TTG	GAA	CAT	AAG	TGT	TTT	CTT
Ile	Ser	Val	Asn	Ser	Gln	Lys	Thr	Lys	Asn	Leu	Val	Phe	Thr	Lys	Glu>
		<b>-</b> 7 ·	2.0			740			750		-	_			
	*	1.	30			740		•	750			76	0		
GAC	ACA	ATA	ACA	GTA	CAA	444	TAC	GAC	TC 4	GCA	GGC -	»CC	ት ጉ	رس. -	GA 3
										CGT					
	Th-	710	The	Val	Gln	Tive	77.2	Asn	Ser	27.	Gly	Th-	2	T	Glu>

FIGURE 28 (2 of 3)

#### B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

770 780 790 800 810

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA

CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT

Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820 AAA TAA TTT ATT Lys ***>

FIGURE 28 (3 of 3)

### B-31 OSPA/ B-31 OSPB FUSION

10		20 .	30	)	40	•	
•		•	•	•	•	• •	
ATG AAA AAA	TAT TTA	TTG GGA	ATA GGT	CTA ATA	TTA GCC	TTA ATA	GCA
APC AND AND	דבב בדב	AAC CCT	TAT CCA	GAT TAT	AAT CGG	AAT TAL	-G I
Met Lys Lys	Tyr Leu	Leu Gly	Ile Gly	Leu Ile	Leu Ala	Leu Ile 2	Ala>
50	60		70	80	•	90 . •	•
TGT AAG CAA	*	>CC >CC	CTT GA	- CAC AA	A AAC AGC	GTT TCA	GTA .
TGT AAG CAA ACA TTC GTT	AAT GII	TCG TCG	GAA CT	CTC TT	TTG TCG	CAA AGT	CAT
Cys Lys Glr	LAC CAR	Ser Ser	Leu Asi	Glu Ly	s Asn Ser	Val Ser	Val>
Cys Dys Gr.				· <del>-</del>			
100	110		120		130	140	
•	•	•	•	*	• •	•	
GAT TTG CC	r ggt gaa	ATG AAA	GTT CT	I GTA AG	C AAA GAA	AAA AAC	AAA ~~~
CTA AAC GG	A CCA CTT	TAC TTT	CAA GA	A CAT TO	s Tre Cli	Tyr her	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Asp Leu Pro	o Gly Glu	Met Lys	val Le	u vai se.	r Lys Gru	Lys Asir.	_y s/
150	3	60	170		180	19	0
•	•	•	•	•	•	•	•
GAC GGC AA	G TAC GAT	CTA ATT	GCA AC	A GTA GA	C AAG CTI	GAG CTT	AAA
כדה ככה דד	C ATG CTA	GAT TAA	CGT TG	T CAT CT	G TTC GAA	CTC GAA	L.I.I.
Asp Gly Ly	s Tyr Asp	Leu Ile	Ala Th	r Val As	p Lys Leu	Glu Leu	Lys>
200		210		220	230		240
200	•	210	•	•	•	•	•
GGA ACT TO	T GAT AAA	AAC AAT	GGA TO	T GGA GT	A CTT GAR	GGC GTA	AAA
CCT TGA AG	A CTA TTT	TTG TTA	CCT AG	A CCT CA	T GAA CT	CCG CAT	TTT
Gly Thr Se	r Asp Lys	Asn Asn	Gly Se	r Gly Va	l Leu Glu	Gly Val	Lys>
•				270		280	
	250	260	•	270 *	•	• •	
GCT GAC A	AGT AAA	GTA AAA	A TTA AC	TTA A	T GAC GAT	CTA GGT	CAA
CGA CTG TT	T TCA TTI	CAT TT	T-AAT-TO	OK KAT TE	SA CTG CT	A GAT CCA	GTT
Ala Asp Ly	s Ser Lys	Val Ly	s Leu Th	r Ile Se	er Asp As	p Leu Gly	Gln>
290	300		310	-320	J ★ <b>*</b>	330	•
ACC ACA C	nn chh car	יים די יויירי אאי	A GAA G	AT GGC A	AA ACA CT	A GTA TCA	AAA
TGG TGT G	LI GAM GI	A AAG TT	T CTT C	TA CCG T	TT TGT GA	T CAT AGT	TIT
Thr Thr Le	eu Glu Val	l Phe Ly	s Glu A	sp Gly L	ys Thr Le	u Val Ser	Lys>
		· -			•		
340	350		360		370	380	
•	•			•	*	* ************************************	643
AAA GTA A	CT TCC AA	A GAC AA	G TCA T	CA ACA G	ለጸ ሁለጸ ጸጸ ጥጥ ርጥጥ ጥሻ	TAA OTT AAT ATT DAA T	CTT
TTT CAT T	GA AGG IT	T CIG TI	C AGI A	er Thr C	lu Glu IN	T AAG TTA 's Phe Asn	Glu>
rys var T	nr ser Ly	P WPD DA	3 261 3	6			

FIGURE 29 (1 of 3)

#### B-31 OSP A/ B-31 OSP B FUSION

		390	-		4	00			410			420	)		2	30.
	•	•		•		•	•		•		•	•		•		•
	AAA	GGT	GAA	GTA	TCT	GAA	AAA	. ATA	ATA	ACA	AGA	GCA	GAC	GGA	ACC	AGA
	TTT	CCA	CTT	CAT	AGA	CII	TTT	TAT	TAT	TGI	, ICI	CGT	, CIG	CCI	ישרי:	TCT
	Lys	GIA	Glu	Val	Ser	Glu	. Lys	Ile	Ile	Thr	Arg	. Ala	Asp	Gly	The	Arg>
			440			450			4	60			470	-		480
	•		•		•	•		•	•	•	. •		*		•	480
	CTT	GAA	TAC	ACA	GGA	ATT	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCT	' AAA	GAG
	GAA	CTT	ATG	TGT	CCT	TAA	TIT	TCG	CTA	CCI	AGA	CCT	TTT	CGA	TTT	CTC
	Leu	Glu	Tyr	Thr	Gly	Ile	Lys	Ser	Asp	Gly	Ser	Cly	Lys	Ala	Lys	Glu>
			4	90			500	•		510			5	20		
		•		•	•		•		•	•		•	_	•	•	
	GTT	TTA	AAA	GGC	TAT	GTT	CTT	GÀA	GGA	ACT	CTA	ACT	GCT	GAA	AAA	ACA
	CAA	TAA	TTT	CCG	ATA	CAA	GAA	CII	CCT	TGA	GAT	TGA	CGA	CTT	TTT	TGT
	Val	Leu	Lys	Gly	Tyr	Val	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys	Thr>
	530			540			5	50			560			570		
	•		•	•		•		•	•.		•		•	•	•	•
	ACA	TTG	GTG	GTT	AAA	GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	AT.	TCA
	TGT	AAC	CAC	CAA	TTT	CTT	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	TAL	ACT
7	Thr	Leu	Val	Val	Lys	Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Asn	Ile	Ser>
	58	30		9	590			600			61	.0			520.	
		•	•		•		• .	•		•		•	•		520.	
	AAA	TCT	GGG	GAA	GTT	TCA	GTT	- GAA	CTT	AAT	GAC	ACT	GAC	AGT	AGT	GCT
	AAA TTT	TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC	ACT TGA	CTG	AGT TCA	AGT	CGA
	AAA TTT	TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC	ACT TGA	CTG	AGT TCA	AGT	GCT CGA Ala>
	AAA TTT	TCT AGA	CCC	GAA CTT	GTT CAA	AGT Ser	CAA	GAA CTT Glu	GAA	TTA	GAC	ACT TGA	CTG	AGT TCA	AGT	CGA Ala>
	AAA TTT Lys	TCT AGA Ser 630	Gly	GAA CTT Glu	GTT CAA Val	AGT Ser	CAA Val	GAA CTT Glu	GAA Leu 50	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
	AAA TTT Lys	TCT AGA Ser 630	CCC	GAA CTT Glu	GTT CAA Val 64	AGT Ser	CAA Val	GAA CTT Glu 6	GAA Leu 50	TTA Asn GAC	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala>
	AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu 6 TGG ACC.	GAA Leu 50 AAT TTA	TTA Asn GAC CTG	GAC CTG Asp -	ACT TGA Thr 660 ACT	CTG Asp AGC TCG.	AGT TCA Ser	AGT TCA Ser 67 TTA	CGA Ala> O ACA
	AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu 6 TGG ACC.	GAA Leu 50 AAT TTA	TTA Asn GAC CTG	GAC CTG Asp -	ACT TGA Thr 660 ACT	CTG Asp AGC TCG.	AGT TCA Ser	AGT TCA Ser 67 TTA	CGA Ala>
	AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu 6 TGG ACC.	GAA Leu 50 AAT TTA	TTA Asn GAC CTG Asp	GAC CTG Asp -	ACT TGA Thr 660 ACT TGA Thr	CTG Asp AGC TCG.	AGT TCA Ser	AGT TCA Ser 67 TTA	CGA Ala> O ACA
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 10 * GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu GG TGG ACC. Trp	GAA Leu 50 AAT TTA. Asn	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT Leu	CGA Ala>  0 ACA TGT Thr> 720
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA-TTT Lys	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 10 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC. TIP	GAA Leu 50 AAT TTA. Asn 70	GAC CTG Asp	GAC CTG ASP AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala>  0 ACA TGT Thr> 720
	AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TTT Lys 680 • GCT	GAA CTT Glu AAA TTT Lys GAC CTG	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 10 GCA CGT Ala 690 AAA TTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC. Trp ACT TGA	GAA Leu 50 AAT TTA. ASD 70 AAA TTT	GAC CTG ASP	GAC CTG Asp AGT TCA Ser TTG AAC	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser 10	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu ACA	CGA Ala>  0 ACA TGT Thr> 720 GAT
	AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TTT Lys 680 • GCT	GAA CTT Glu AAA TTT Lys GAC CTG	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 10 GCA CGT Ala 690 AAA TTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC. Trp ACT TGA	GAA Leu 50 AAT TTA. ASD 70 AAA TTT	GAC CTG ASP	GAC CTG Asp AGT TCA Ser TTG AAC	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser 10	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu ACA	CGA Ala>  0 ACA TGT Thr> 720
	AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TTT Lys 680 • GCT	GAA CTT Glu AAA TTT Lys GAC CTG ASP	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser IO GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC. Trp ACT TGA	GAA Leu 50 AAT TTA. ASD 70 AAA TTT	GAC CTG ASP	GAC CTG Asp AGT TCA Ser TTG AAC	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser 10	AGT TCA Ser ACT TGA Thr TTA AAT Leu	AGT TCA Ser 67 TTA AAT Leu ACA	CGA Ala>  0 ACA TGT Thr> 720 GAT
	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser	AAA TTT Lys 80 GCT CGA Ala	GAA CTT Glu AAA TTT Lys GAC CTG Asp	GTT CAA Val 64 ACT TGA Thr AGC TCG Ser	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC. Trp ACT TGA Thr	GAA Leu 50 AAT TTA ASD 70 AAA TTT Lys	GAC CTG ASP 0 GAT CTA ASP	GAC CTG Asp AGT TCA Ser TTG AAC Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	AGC TCG Ser 10 TTC AAG Phe 76	AGT TCA Ser ACT TGA Thr TTA AAT Leu	AGT TCA Ser 67 TTA AAT Leu ACA TGT Thr	CGA Ala>  0 ACA TGT Thr> 720 GAT CTA ASP>
	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser	AAA TTT Lys 80 GCT CGA Ala 73	GAA CTT Glu AAA TTT Lys GAC CTG ASP	GTT CAA Val 64 ACT TGA Thr AGC TCG Ser GTA	AGT Ser IO GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC. Trp ACT TGA Thr	GAA Leu 50 AAT TTA ASD 70 AAA TTT Lys	GAC CTG ASP 0 GAT CTA ASP 750	GAC CTG Asp AGT TCA Ser TTG AAC Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	AGC TCG Ser 10 TTC AAG Phe 76	AGT TCA Ser ACT TGA Thr TTA AAT Leu	AGT TCA Ser 67 TTA AAT Leu ACA TGT Thr	CGA Ala>  0 ACA TGT Thr> 720 GAT CTA Asp>
	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACA TGT	AAA TTT Lys 80 GCT CGA Ala 73 ATT	GAA CTT Glu AAA TTT Lys GAC CTG ASP	GTT CAA Val 64 ACT TGA Thr AGC TCG Ser GTA CAT	AGT Ser 0 GCA CGT Ala 690 AAA TTT Lys 7 CAA GTT	CAA Val GCT CGA Ala AAA TTT Lys 40	GAA CTT Glu TGG ACC. Trp ACT TGA Thr	GAA Leu 50 AAT TTA ASD 70 AAA TTT Lys	GAC CTG ASP 0 GAT CTA ASP 750 ACA	GAC CTG Asp AGT TCA Ser TTG AAC Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	AGC TCG Ser 10 TTC AAG Phe ACC TGG	AGT TCA Ser ACT TGA Thr TTA AAT Leu AGC	AGT TCA Ser 67 TTA AAT Leu ACA TGT Thr	CGA Ala>  0 ACA TGT Thr> 720 GAT CTA Asp>

FIGURE 29 (2 of 3)

#### B-31 OSP A/ B-31 OSP B FUSION

770 780 790 800 810

GGA TCA GCA AGT GAA ATT AAA AAT CTT TCA GAG CTT AAA AAC GCT TTA

CCT AGT CGT TCA CTT TAA TTT TTA GAA AGT CTC GAA TTT TTG CGA AAT

Gly Ser Ala Ser Glu Ile Lys Asn Leu Ser Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys ***>

#### B-31 OSP A/ B-31 OSP B / B-31 OSP C FUSION

nce Range: 1 to 1401

		:	10			20			30				40	•	
	•		•			•		•	•				•	•	
	AAA														
															CGT Ala>
. Met	Lys	Lys	171	Leu	Deu	Gly	116	Gry	Deu	116	Deu	Ald	Leu	116	ATS>
50			60			. 7	70			80			90		
•		*	•		•		•	•		•		•	•		•
	AAG														
	TTC														
Cys	Lys	Gin	ASN	Vai	Ser	ser	Leu	ASP	GIU	Lys	ASN	ser	vai	Ser	Val>
1	00		1	110			120			1:	30			140	
	•	•		•		•	•		•		•	•		•	
	TTG														
	AAC														
Asp	Leu	Pro	Gly	Glu	Met	Lyś	Val	Leu	Val	Ser.	Lys	Glu	Lys	Asn	Lys>
	150			16	50			170			180			1 9	<b>9</b> 0
•	•	×	•		•	•		•		•	•		•		•
GAC	GGC	AAG	TAC	GAT	CTA	TTA	GCA ^r	ACA	GTA	GAC	AAG	CTT	GAG	CTT	AAA
CTC	CCG	TTC	ATG	CTA	GAT	TAA	CGT	TGT	CAT	CTG	TTC	GAA	CTC	GAA	TIT
Asp	Gly	Lys	Tyr	Asp	Leu	Ile	Ala	Thr	Val	Asp	Lys	Leu	Glu	Leu	Lys>
	:	200			210			22	20		2	230			240
. •		•		•	•		•		• ,	•		•		•	•
	ACT	• TCT			AAC			TCT	• GGA		CTT	• Gaa			AAA
CCI	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTA	CCT	TCT AGA	• GGA	CAT	CTT GAA	GAA CTT	CCG	CAT	AAA TTT
CCI	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTA	CCT	TCT AGA	• GGA	CAT	CTT GAA	GAA CTT	CCG	CAT	AAA
CCI	ACT TGA	TCT AGA Ser	CTA	TTT	AAC TTG Asn	TTA	CCT	TCT AGA	• GGA	CAT	CTT GAA	GAA CTT	CCG Gly	CAT	AAA TTT
CC1 Gly	ACT TGA Thr	TCT AGA Ser	CTA Asp 50	TTT Lys	AAC TTG Asn	TTA Asn 260	CCT	TCT AGA Ser	GGA CCT Gly 270	CAT Val	CTT GAA Leu	GAA CTT Glu 28	CCG Gly 80	CAT Val	AAA TTT Lys>
GCT GLY	ACT TGA Thr	TCT AGA Ser 25	CTA Asp 50 * AGT	TTT Lys	AAC TTG ASD	TTA Asn 260 AAA	CCT Gly TTA	TCT AGA Ser	GGA CCT Gly 270	CAT Val	CTT GAA Leu GAC	GAA CTT Glu 28	CCG Gly 80 • CTA	CAT Val	AAA TTT Lys>
GCT GLY GCT CG3	ACT TGA Thr GAC	TCT AGA Ser 2! AAA TTT	CTA Asp 50 AGT TCA	TTT Lys AAA TTT	AAC TTG ASD GTA CAT	TTA ASD 60 AAA TTT	CCT Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 28 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys>
GCT GLY GCT CG3	ACT TGA Thr GAC	TCT AGA Ser 2! AAA TTT	CTA Asp 50 AGT TCA	TTT Lys AAA TTT	AAC TTG ASD GTA CAT	TTA ASD 60 AAA TTT	CCT Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 28 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys>
GCT GLY GCT CG3	ACT TGA Thr GAC	TCT AGA Ser 2! AAA TTT	CTA Asp 50 AGT TCA	TTT Lys AAA TTT	AAC TTG ASD GTA CAT	TTA ASD 260 AAA TTT Lys	CCT Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 28 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys>
GCT GGA Ala	ACT TGA Thr GAC CTG	TCT AGA Ser 2! AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300	TTT Lys AAA TTT Lys	AAC TTG Asn GTA CAT Val	AAA TTT Lys	CCT Gly TTA AAT Leu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA Ser	CTT GAA Leu GAC CTG Asp	GAA CTT Glu 28 GAT CTA Asp	CCG Gly 30 CTA GAT Leu 330	CAT Val GGT CCA Gly	AAA TTT Lys> CAA GTT Gln>
GCT GGA Ala	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2! AAA TTT Lys	CTA ASP  O  AGT TCA Ser  300 GAA	TTT Lys AAA TTT Lys	AAC TTG Asn GTA CAT Val	TTA ASN 260 AAA TTT Lys 33	CCT Gly TTA AAT Leu 10	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320	CTT GAA Leu GAC CTG Asp	GAA CTT Glu 28 GAT CTA Asp	CCG Gly 30 CTA GAT Leu 330	CAT Val GGT CCA Gly	AAA TTT Lys> CAA GTI Gln>
GCT GCA Ala 290	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2! AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT	TTT Lys AAA TTT Lys GTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT  AAA TTT  AAA TTT	CCT Gly TTA AAT Leu 10	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GGC CCG	TCT AGA Ser 320	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 28 GAT CTA ASD	CCG Gly 30 CTA GAT Leu 330 GTA CAT	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GCT GCA Ala 290	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2! AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT	TTT Lys AAA TTT Lys GTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT  AAA TTT  AAA TTT	CCT Gly TTA AAT Leu 10	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GGC CCG	TCT AGA Ser 320	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 28 GAT CTA ASD	CCG Gly 30 CTA GAT Leu 330 GTA CAT	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTI Gln>
GCT Gly GCT CG# Ala 290 * ACC Thi	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2! AAA TTT Lys	AGT TCA Ser 300 GAA CTT Glu	TTT Lys AAA TTT Lys GTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT  AAA TTT  AAA TTT	CCT Gly TTA AAT Leu 10	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GGC CCG	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 28 GAT CTA ASD	CCG Gly 30 CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GCT Gly GCT CGA Ala 290 * ACC Thi	ACT TGA Thr GAC CTG ASP ACA TGT Thr	TCT AGA Ser  2: AAA TTT Lys  CTT GAA Leu	AGT TCA Ser 300 GAA CTT Glu	TTT Lys  AAA TTT Lys  GTT CAA Val	AAC TTG Asn GTA CAT Val TTC AAG Phe	TTA ASD 260 AAA TTT Lys AAA TTT Lys	CCT Gly TTA AAT Leu GAA CTT Glu 360	TCT AGA Ser ACA TGT Thr GAT CTA Asp	GGA CCT Gly 270 ATT TAA Ile GGC CCG Gly	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG Asp ACA TGT Thr	GAA CTT Glu 28 GAT CTA Asp CTA GAT Leu	CCG Gly 0 * CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT Ser	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>
GCT Gly GCT CGA Ala 290 TGC Thi	ACT TGA Thr GAC CTG ASP ACA TGT Thr	TCT AGA Ser 2: AAA TTT Lys CTT GAA Leu ACT	CTA ASP 50 AGT TCA Ser 300 GAA CTT Glu TCC	TTT Lys  AAA TTT Lys  GTT CAA Val  350 AAA	AAC TTG Asn GTA CAT Val TTC AAG Phe	TTA ASD 260 AAA TTT Lys AAA TTT Lys AAA AAA TTT Lys	CCT Gly TTA AAT Leu 10 GAA CTT Glu 360	TCT AGA Ser ACA TGT Thr GAT CTA ASP	GGA CCT Gly 270 ATT TAA Ile GGC CCG Gly	TCT AGA Ser 320 AAA TTT Lys 3° GAA	CTT GAA Leu GAC CTG ASP ACA TGT Thr	GAA CTT Glu 28 GAT CTA Asp CTA GAT Leu	CCG Gly 30 CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT Ser	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>
GCT Gly GCT CGA Ala 290 * ACC Thi	ACT TGA Thr GAC CTG ASP ACA TGT Thr GTA	TCT AGA Ser  2: AAA TTT Lys  CTT GAA Leu  ACT TGA	AGT TCA Ser 300 GAA CTT Glu	TTT Lys  AAA TTT Lys  GTT CAA Val  350  AAA TTT	AAC TTG ASD GTA CAT Val TTC AAG Phe	TTA ASD 60 AAA TTT Lys AAA TTT Lys AAG TTC	CCT Gly TTA AAT Leu 10 GAA CTT Glu 360 TCA	TCT AGA Ser ACA TGT Thr CTA ASP	GGA CCT Gly 270 ATT TAA Ile GGC CCG Gly	TCT AGA Ser 320 AAA TTT Lys 3° GAA CTT	CTT GAA Leu GAC CTG ASP ACA TGT Thr	GAA CTT Glu 28 GAT CTA ASP CTA GAT Leu	CCG Gly 30 CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT Ser 80 AAT	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>

FIGURE 30 (1 of 4)

### B-31 OAP A/ B-31 OSP B / B-31 OSPC FUSION

390		400		4	10			420			4 3	S Ó
•	•	•	•		•		*	•		•		•
aaa ggt gaa	GTA TC	T GAA	AAA	ATA .	ATA	ACA	AGA	GCA	GAC	GGA	ACC	AGA
TTT CCA CTT Lys Gly Glu	CAT AG	A CTT	TIT	TAT T	TAT	The	TCI Arm	Ala	Acn	CLT	The	ATO.
Lys Gly Glu	val se	r GIU	Lys	116	116	1111	vr a	7.6	vah	GLY	* * * * *	AL Y
440		450		•	46	0		4	70			480
•	•	•		•		•	•		•		•	•
CTT GAA TAC	ACA GG	TTA A	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCT	AAA	GAG
GAA CTT ATG	TGT CC	AAT T	TTT	TCG	CTA	CCT	AGA	CCI	TTT	CGA	TIT	CIC
Leu Glu Tyr	Thr Gl	y Ile	Lys	Ser	Asp	Gly	Ser	Gly	Lys	Ala	Lys	Glu>
49	20	c	500			510			52	20		
•	•	• .	•		•	•		•		•	•	
GTT TTA AAA	GGC TA	T GTT	CTT	GAA	GGA	ACT	CTA	ACT	GCT	GAA	AAA	ACA
CAA AAT TTT	CCG AT	TA CAA	GAA	CTT	CCT	TGA	GAT	TGA	CGA	CIT	TII	TGT
Val Leu Lys	GJA 17	r Val	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys	Thr>
530	540		55	50		9	560			570		
± ±	•	•	-	•	•		•		•	•		. •
ACA TTG GTG	GTT A	AA GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	ATT	TCA
TGT AAC CAC	CAA T	TT CTT	CCT	TGA	CAA	TGA	TAA	TCG	TIT	TTA	TAA	AGT
Thr Leu Val	Val Ly	ys Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Asn	Ile	Ser>
580	590	0		600			6	10		,	620	
580	59	•	•	600		•		•	•		•	
AAA TCT GGG	GAA G	· TT TCA	• GTT	• GAA	CTT	· AAT	GAC	• ACT	- GAC	AGT	AGT	GCT
AAA TCT GGG	GAA G' CTT C	· TT TCA AA AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TCT GGG	GAA G' CTT C	· TT TCA AA AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TCT GGG TTT AGA CCC Lys Ser Gly	GAA G' CTT C	TT TCA AA AGT al Ser	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA Ala>
AAA TCT GGG TTT AGA CCC Lys Ser Gly	GAA G CTT C Glu V	TT TCA AA AGT al Ser	CAA Val	GAA CTT Glu	GAA Leu 650	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA	GAA G' CTT C Glu V	TT TCA AA AGT al Ser 640 CT GCA	CAA Val	GAA CTT Glu TGG	GAA Leu 650 AAT	TTA Asn GAC	GAC CTG Asp	ACT TGA Thr 660	ASP AGC	AGT TCA Ser	AGT TCA Ser 6	CGA Ala> 70 ACA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT	GAA G'CTT C	TT TCA AA AGT al Ser 640 CT GCA GA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT	TTA Asn GAC CTG	GAC CTG Asp AST	ACT TGA Thr 660 ACT	ASP AGC TCG	AGT TCA Ser ACT TGA	AGT TCA Ser 6 TTA AAT	CGA Ala> 70 ACA TGT
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA	GAA G'CTT C	TT TCA AA AGT al Ser 640 CT GCA GA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT	TTA Asn GAC CTG	GAC CTG Asp AST	ACT TGA Thr 660 ACT	ASP AGC TCG	AGT TCA Ser ACT TGA	AGT TCA Ser 6 TTA AAT	CGA Ala> 70 ACA TGT
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT	GAA G'CTT C	TT TCA AA AGT al Ser 640 CT GCA GA CGT	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA Asn	TTA Asn GAC CTG	GAC CTG Asp AST	ACT TGA Thr 660 ACT TGA Thr	ASP AGC TCG	AGT TCA Ser ACT TGA	AGT TCA Ser 6 TTA AAT	CGA Ala> 70 ACA TGT
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT Ala Thr Lys	GAA G'CTT CA	TT TCA AA AGT al Ser  640 CT GCA GA CGT hr Ala	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA Asn	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT Ala Thr Lys  680 ATT AGT GCT	GAA G'CTT CAGA CAGA CAGA CAGA CAGA CAGA CAGA C	TT TCA AA AGT al Ser  640 CT GCA GA CGT hr Ala  690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA ASD	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA CGA TGA TTT Ala Thr Lys  680  ATT AGT GCT TAA TCA CGA	GAA G' CTT CA Glu VA AAA A TTT T Lys T GAC A CTG T	TT TCA AA AGT al Ser  640 CT GCA GA CGT hr Ala  690 AGC AAA	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC TIP	GAA Leu 650 AAT TTA Asn 7	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr CGA CCAC	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT Ala Thr Lys  680 ATT AGT GCT	GAA G' CTT CA Glu VA AAA A TTT T Lys T GAC A CTG T	TT TCA AA AGT al Ser  640 CT GCA GA CGT hr Ala  690 AGC AAA	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC TIP	GAA Leu 650 AAT TTA Asn 7	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr CGA CCAC	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT Ala Thr Lys  680 ATT AGT GCT TAA TCA CGA	GAA G' CTT CA Glu VA AAA A TTT T Lys T GAC A CTG T	TT TCA AA AGT al Ser  640 CT GCA GA CGT hr Ala  690 AGC AAA	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC TIP	GAA Leu 650 AAT TTA Asn 7	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr CGA CCAC	AGC TCG Ser 710 TTCC AAGC	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA CGA TGA TTT Ala Thr Lys  680  ATT AGT GCT TAA TCA CGA Ile Ser Ala	GAA G' GIU V' AAA A' TTT T Lys T GAC A CTG T ASP S	TT TCA AA AGT al Ser 640 CT GCA GA CGT hr Ala 690 AGC AAA CG TTI Ser Lys	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7 AAA TTT Lys	GAC CTG Asp 00 GAT CTA Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr CGC CAC	AGC TCG Ser 710 TTC AAG	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu ACA	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA Asp>
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA CGA TGA TTT Ala Thr Lys  680  ATT AGT GCT TAA TCA CGA Ile Ser Ala	GAA G' GIU V' AAA A' TTT T Lys T GAC A CTG T AASP S	TT TCA AA AGT al Ser 640 CT GCA GA CGT hr Ala 690 AGC AAA CGT TTS	CAA Val GCT CGA Ala AAA TTT Lys 740	GAA CTT Glu TGG ACC Trp ACT TGA	GAA Leu 650 AAT TTA ASD 7 AAA TTT Lys	GAC CTG ASP 00 CTA CTA ASE 750	GAC CTG Asp AGT TCA Ser TTC AAC Lev	ACT TGA Thr 660 ACT TGA Thr CGA Thr	AGC TCG Ser 710 TTC AAG	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu ACA TGT	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA ASP> A GAA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA CGA TGA TTT Ala Thr Lys  680  ATT AGT GCT TAA TCA CGA Ile Ser Ala	GAA G' GIU V' AAA A' TTT T Lys T ACA CA A TGT C	TT TCA AA AGT al Ser 640 CT GCA GA CGT hr Ala 690 CGC AAA CGC TTI Ser Lys	CAA Val GCT CGA Ala AAA TTTT Lys 740 A CAA	GAA CTT Glu TGG ACC Trp ACT TGA	GAA Leu 650 AAT TTA Asn 7 AAA TTTI Lys	GAC CTG ASP OO CTA CTA ASP 750 CACA CTG TGC	GAC CTG Asp AGT TCA Ser TCA AAC Lev	ACT TGA Thr 660 ACT TGA Thr CGGGGA CCG	AGC TCG Ser 710 AACC TCG TCG	AGT TCA Ser ACT TGA Thr TAAT Leu 60	AGT TCA Ser 6 TTA AAT Leu ACA TGT Thx	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA ASP> A GAA CTT

FIGURE 30 (2 of 4)

#### B-31 OSP A/ B-31 OSP B / B-31 OSP C FUSION

770			780			7	90			800			81(	1	
•		•	•		•		•	•		•		•	•	•	•
GGA	TCA	GCA	AGT	GAA	ATT	AAA	AAT	CTI	TCA	GAG	CTI	· AAA	. AAC	GCI	TTA
CCI	, AGI	CGT	TCA	CTT	TAA	TTT	TTA	. Gaa	AGI	, CIC	GAA	777	770	: (6:	227
Gly	Ser	Ala	Ser	Glu	Ile	Lys	Asn	Leu	Ser	Glu	Leu	Lys	Às:	: Ala	Leu>
8	20			830			840			8	50			550	
	•			•		• .	•		•		•	•		•	•
AAA	ATG	GCT	AAT	AAT	TCA	GGG	AAA	GAT	GGG	AAT	ACA	TCT	GCA	TAA .	ICI
111	MAC	LUA	TTA	TTA	AGT	600	TTT	CTA	CCC	TTA	TGT	AGA	CGI	TTA	AGA
Lys	nec	VIG	ASII	ASII	ser	GIY	Lys	Asp	GTÅ	ASD	-Thr	Ser	Ala	Asn	Ser>
	870			8	80		1	890 [°]			900			9	10
•	•		•		•	•		•		•	•		•		•
GCT	GAT	GAG	TCT	GTT	AAA	GGG	CCT	AAT	CTT	ACA	GAA	ATA	AGT	AAA	ሕሕሕ
CGA	CTA	CIC	AGA	CAA	TTT	CCC	GGA	TTA	GAA	TCT	CTT	TAT	TCA	TIT	III
Ala	Asp	Glu	Ser	Val	Lys	Gly	Pro	Asn	Leu	Thr	Glu	Ile	Ser	Lys	_ys>
	. 9	920			930			9	4 D		9	950			960
•		•	•	•	*		•		•	•		•		•	•
ATT	ACG	GAT	TCT	AAT	GCG	GTT	TTA	CTT	GCT	GTG	AAA	GAG	GTT	GAA	G-CG
TAA	TGC	CTA	AGA	TTA	CGC	CAA	AAT	GAA	CGA	CAC	TTT	CTC	CAA	CTT	CGC
*:TIE	Thr	ASP	Ser	Asn	Ala	Val	Leu	Leu	Ala	Val	Lys	Glu	Val	Glu	Ala>
₫³.		Q.	70			980			990						
	•		•	•	•	•		•	*		. • •	100	00	_	
		202	TCT	ATA	GAT	GAA	ATT	GCT	GCT	AAA	GCT	ATT	CCT	AAA	223
TTG	CTG	ICA													~~~
· AAC	GAC	AGT	AGA	TAT	CTA	CIT	TAA	CGA	CGA	TTT	CGA	TAL	CC3	للسلمك	للثثث
TTG AAC Leu	GAC	AGT	AGA	TAT	CTA	CIT	TAA	CGA	CGA	TTT	CGA	TAL	CC3	للسلمك	TTT Lys>
· AAC	GAC	AGT Ser	AGA	TAT	CTA	CIT	TAA Ile	CGA	CGA Ala	TTT	CGA	TAA Ile	CCA	للسلمك	TTT Lys>
E O10	Leu	AGT Ser	AGA Ser	TAT Ile	CTA Asp	Glu 103	TAA Ile O	CGA Ala	CGA Ala 10	TTT Lys	CGA Ala	TAA Ile	CCA Gly 050	TTT Lys	Lys>
PAAC Leu 1010 ATA	CAC	AGT Ser	AGA Ser 1020	TAT Ile	CTA Asp	CTT Glu 103 TTG	TAA Ile 0	CGA Ala	CGA Ala 10 GAA	TTT Lys 40	CGA Ala	TAA Ile	CCA Gly .050	TTT	Lys>
PAAC Leu 010 ATA TAT	CAC GTG	AGT Ser CAA GTT	AGA Ser 1020 AAT TTA	TAT Ile AAT TTA	CTA Asp GGT CCA	CTT Glu 103 TTG AAC	TAA Ile 0 + GAT CTA	CGA Ala * ACC TGG	CGA Ala 10 GAA CTT	Lys 40 TAT	CGA Ala AAT TTA	TAA Ile ' CAC GTG	CCA Gly 050 AAT	TTT Lys GGA	Lys> TCA
PAAC Leu 010 ATA TAT	CAC GTG	AGT Ser CAA GTT	AGA Ser 1020 AAT TTA	TAT Ile AAT TTA	CTA Asp GGT CCA	CTT Glu 103 TTG AAC	TAA Ile 0 + GAT CTA	CGA Ala * ACC TGG	CGA Ala 10 GAA CTT	Lys 40 TAT	CGA Ala AAT TTA	TAA Ile ' CAC GTG	CCA Gly 050 AAT	TTT Lys GGA	Lys>
PAAC Leu 010 ATA TAT	CAC GTG His	AGT Ser CAA GTT	AGA Ser LO20 AAT TTA Asn	TAT Ile AAT TTA	CTA Asp GGT CCA	CTT Glu 103 TTG AAC Leu	TAA Ile 0 + GAT CTA	CGA Ala * ACC TGG	CGA Ala 10 GAA CTT	Lys 40 TAT	CGA Ala AAT TTA Asn	TAA Ile ' CAC GTG	CCA Gly 050 AAT TTA Asn	TTT Lys GGA	Lys> TCA
ATA TAT Lie	CAC GTG His	Ser CAA GTT Gln	AGA Ser 1020 AAT TTA Asn	TAT Ile AAT TTA Asn	CTA Asp GGT CCA Gly	CTT Glu 103 TTG AAC Leu	TAA Ile 0 GAT CTA ASP	ACC TGG Thr	CGA Ala 10 GAA CTT Glu	TTT Lys 40 TAT ATA Tyr	CGA Ala AAT TTA Asn	TAA Ile CAC GTG His	CCA Gly 050 AAT TTA Asn	TTT Lys GGA CCT Gly	Lys> TCA AGT Ser>
AAC Leu 1010 ATA TAT Ile 106	CAC GTG His	AGT Ser CAA GTT Gln	AGA Ser 1020 AAT TTA Asn 10	AAT TTA Asn CGT	GGT CCA Gly	CTT Glu 103 TTG AAC Leu 1 GCA	TAA Ile 0 GAT CTA ASP 080	CGA Ala ACC TGG Thr	CGA Ala 10 GAA CTT Glu	TTT Lys 040 TAT ATA Tyr 109	CGA Ala AAT TTA Asn 0	TAA Ile CAC GTG His	CCA Gly 050 AAT TTA ASD	TTT Lys GGA CCT Gly	Lys> TCA AGT Ser>
AAC Leu LO10 ATA TAT LILE LO6 TTG AAC	CAC GTG His_	AGT Ser CAA GTT Gln GCG CGC	AGA Ser 1020 AAT TTA Asn 10	AAT TTA ASD CGT GCA	GGT CCA Gly TAT	CTT Glu 103 TTG AAC Leu 1 GCA CGT	TAA Ile 0 GAT CTA ASP 080 ATA	CGA Ala ACC TGG Thr TCA AGT	CGA Ala 10 GAA CTT Glu ACC TGG	TTT Lys  40 TAT ATA Tyr  109 CTA GAT	AAT TTA ASD  ATA	TAA Ile  CAC GTG His	CCA Gly 050 AAT TTA ASD 11	TTT Lys GGA CCT Gly 00 AAA	Lys> TCA AGT Ser> TTA
AAC Leu	CAC GTG His TTA AAT Leu	AGT Ser CAA GTT Gln GCG CGC	AGA Ser 1020 AAT TTA Asn 10	AAT TTA ASD TO CGT GCA Arg	GGT CCA Gly TAT ATA Tyr	CTT Glu 103 TTG AAC Leu 1 GCA CGT	TAA Ile 0 GAT CTA ASP 080 ATA	CGA Ala ACC TGG Thr TCA AGT	CGA Ala 10 GAA CTT Glu ACC TGG	TTT Lys  40 TAT ATA Tyr  109 CTA GAT	AAT TTA ASD  ATA	TAA Ile  CAC GTG His	CCA Gly 050 AAT TTA ASD 11	TTT Lys GGA CCT Gly 00 AAA	Lys> TCA AGT Ser>
AAC Leu	CAC GTG His_	AGT Ser CAA GTT Gln GCG CGC	AGA Ser 1020 AAT TTA Asn 10	AAT TTA ASD CGT GCA	GGT CCA Gly TAT ATA Tyr	CTT Glu 103 TTG AAC Leu 1 GCA CGT	TAA Ile  O * GAT CTA ASP  O80 * ATA TAT Ile	CGA Ala ACC TGG Thr TCA AGT	CGA Ala 10 GAA CTT Glu ACC TGG	TTT Lys 40 TAT ATA Tyr 109 CTA GAT Leu	AAT TTA ASD  ATA	TAA Ile  CAC GTG His	CCA Gly 050 AAT TTA ASD 11	TTT Lys GGA CCT Gly 00 AAA	Lys> TCA AGT Ser> TTA AAT Leu>
AAC Leu  ATA TAT Ile  106  TTG AAC Leu	CAC GTG His TTA AAT Leu	CAA GTT Gln GCG CGC Ala	AGA Ser 1020 AAT TTA ASD 10 GGA CCT Gly	AAT TTA ASD CGT GCA Arg	GGT CCA Gly TAT ATA Tyr	TTG AAC Leu  GCA CGT Ala	TAA Ile  O * GAT CTA ASP  O80 ATA TAT Ile	ACC TGG Thr TCA AGT Ser 30	GAA GAA CTT Glu • ACC TGG Thr	TTT Lys 40 TAT ATA Tyr 109 CTA GAT Leu	AAT TTA ASD  ATA TAT Ile  140	TAA Ile  CAC GTG His  AAA TTT Lys	CCA Gly .050 *AAT TTA ASN !! CAA GTT Gln	GGA CCT Gly 00 AAA TTT Lys	TCA AGT Ser> TTA AAT Leu>
AAC Leu  ATA TAT Ile  106  TTG AAC Leu  GAT	CAC GTG His TTA AAT Leu	CAA GTT Gln GCG CGC Ala	AGA Ser 1020 AAT TTA ASD 10 GGA CCT Gly	AAT TTA ASD TO CGT GCA Arg 112 AAT	GGT CCA Gly TAT ATA Tyr	TTG AAC Leu  GCA CGT Ala  GGA	TAA Ile  O GAT CTA ASP  OBO ATA TAT Ile  Il	ACC TGG Thr TCA AGT Ser 30	GAA CTT Glu ACC TGG Thr	TTT Lys  40 TAT ATA TYT  109 CTA GAT Leu  1	AAT TTA ASD ATA TAT Ile 140 ATT	TAA Ile  CAC GTG His  AAA TTT Lys	CCA Gly .050 AAT TTA ASN .11 CAA GTT Gln	GGA CCT Gly 00 AAA TTT Lys	TCA AGT Ser> TTA AAT Leu>
AAC Leu O10 ATA TAT Ile 106 AAC Leu CATA CTA	CAC GTG His_ O TTA AAT Leu 110 GGA CCT	CAA GTT Gln GCG CGC Ala	AGA Ser 1020 AAT TTA Asn 10 GGA CCT Gly AAA TTT	AAT TTA ASD CGT GCA Arg 112 AAT TTA	GGT CCA Gly TAT ATA TYr 0 GAA CTT	TTG AAC Leu  GCA CGT Ala  GGA CCT	TAA Ile  O * GAT CTA ASP  OBO ATA TAT Ile  11 TTA AAT	ACC TGG Thr TCA AGT Ser 30 AAG TTC	GAA CTT Glu  ACC TGG Thr	TTT Lys 40 TAT ATA Tyr 109 CTA GAT Leu	AAT TTA ASD  ATA TAT Ile  140 ATT TAA	TAA Ile CAC GTG His AAA TTT Lys	CCA Gly 050 AAT TTA ASD 11 CAA GTT GID	GGA CCT Gly 00 AAA TTT Lys	TTA AAT Leu>  0 AAG

FIGURE 30 (3 of 4)

### B-31 OSP A / B-31 OSP B/ B-31 OSP C FUSION

	11	.60		1	170			118	10		11	.90		ו	200
				•	•		•		*	*		•		•	•
AAA	TGT	TCT	GAA	ACA	TTT	ACT	TAA	AAA	TTA	AAA	GCA	AAA	CAC	ACA	GAT
مسمح	202	ACA	CTT	TGT	AAA	TGA	TTA	TTT	AAT	TTT	CGT	1.1.1.	616	161	CIA
Lys	Cys	Ser	Glu	Thr	Phe	Thr	Asn	Lys	Leu	Lys	Ala	Lys	His	Thr	Asp>
					, -	220		,	230			124	0		
		12:	10	_	4.2	.20					*		•	•	
	•		•	•								C) }		P 42-42	eren y
CTT	GGT	AAA	GAA	GGT	GTT	ACT	GAT	GCT	GAT	GCA	AAA	GAA	900	All	117
GAA	CCA	TTT	CTT	CCA	CAA	TGA	CTA	CGA	CTA	CGT	J-I-I.	CTT	CGG	TAA	AAT
Leu	Gly	Lys	Glu	Gly	Val	Thr	Asp	Ala	Asp	Ala-	Lys	Glu	Ala	Ile	Leu>
									_						
1250			1260			12	70		1	280		. •	1290		_
*		•	•		•		•	*		. •		*	•		•
AAA	ACA	AAT	GGT	ACT	AAA	ACT	AAA	GGT	GCT	GAA	GAA	CII	GGA	AAA	TTA
شكمك	TOTAL TOTAL	<b>ምተ</b> አ	CCA	TGA	TTT	TGA	TTT	CCA	CGA	CTT	CTT	GAA	CCT	TIT	AAT
Lvs	Thr	Asn	Gly	Thr	Lys	Thr	Lys	Gly	Ala	Glu	Glu	Leu	Gly	Lys	Leu>
-															
13	00		1	310		•	1320			13	30		1:	340	
	•	•		•		•	•		•		•	•		•	
עידיד	CAN	TCA	GTA	GAG	GTC	TTG	TCA	AAA	GCA	GCT	AAA	GAG	ATG	CTT	GCT
227	CTT	· AGT	CAT	CTC	CAG	AAC	AGT	, LLL	CGI	, CGY	TTT	CTC	TAC	GAA	CGA
Phe	Glu	Ser	Val	Glu	Val	Leu	Ser	Lys	Ala	Ala	Lys	Glu	Met	Leu	Ala>
														13	
	1350	)		13	60		1	.370			1380		_	13.	-
•	•	•	. •		•	•		•		•	•				
AAT	TC	A GT	KAA 1	GAC	CTI	ACA	AGC	CCI	GTT	GTG	GCA	GAA	AGT	CCA	AAA
ጥተን	א אכי	ר כא	TTT	CTC	GAA	TGI	TCC	GG?	CA	A CAC	: CGT	CTT	TCA	GGT	T.L.L
Asr	Se	r Va	i Lys	Gli	Lèv	Thi	Ser	Pro	Va:	l Val	. Ala	Glu	Ser	Pro	Lys>

1400

AAA CCT TAA TTT GGA ATT Lys Pro ***>

FIGURE 30 (4 of 4)

# B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

				10			20			30	)			40		
		•		•	•	•	•	•	•	•	•	•		•	•	•
	ATG	AAA	AAC	AA1	ACA	ATT A	AGI	CCC	ATA	TTA	ATC	AC:	TT!	TI	TT	A TTT
	TAC	TTI	TTC	TTA	TGI	TAA T	TCA	CGC	TAT	TAA '	TAC	TG	AA?	LAA 1	AA7	AAA
	Met	Lys	Lys	AST	Thr	Leu	Ser	Ala	Ile	Leu	Met	Thi	Lei	Phe	Lei	Phe>
	50			60				70			80			90	)	
	•		•	•		•		•	•		•		•	•		•
	ATA	TCT	TGI	` AAT	TAA	TCA	GGG	AAA	GAT	GGG	AAT	, YC	TCI	` GCA	AAT	TCT
	TAT	AGA	. ACA	. TTA	TTA	AGT	CCC	TTT	CTA	CGC	TTA	-TGI	' AGA	CGT	מדיד	803
	Ile	Ser	Cys	Asn	Asn	Ser	Gly	Lys	Asp	Gly	Asn	Thr	Ser	Ala	Asn	Ser>
	1	00			110	•		120			. 1	30			140	
		•	•		•		•	•		•		•	•			
	GCT	GAT	GAG	TCT	GTT	AAA	GGG	CCT	AAT	CTT	ACA	GAA	ATA	AGT	AAA	AAA
	CGA	CTA	CTC	ÀGA	CAA	TTT	CCC	GGA	TTA	GAA	TGT	CTT	TAT	TCA		شصس
	Ala	Asp	Glu	Ser	Val	Lys	Gly	Pro	Asn	Leu	Thr	Glu	Ile	Ser	Lys	Lys>
		150			1	60			170			180			1	0.0
	• .	•		•		•	•		*		•	*		•		90
ন	ATT	ACG	GAT	TCT	AAT	GCG	GTT	TTA	CTT	GCT	GTG	AAA	GAG	GTT	GAA	GCG
	TAA	TGC	CTA	AGA	TTA	CGC	CAA	AAT	GAA	CGA	CAC	TTT	CTC	CAA	حكت	CGC
	Ile	Thr	Asp	Ser	Asn	Ala	Val	Leu	Leu	Ala	Val	Lys	Glu	Val	Glu	Ala>
			200		•	210			2	20			230			243
e e	•		•		•	. •		•		•	•		•		•	•
	TTG	CTG	TCA	TCT	ATA	GAT	GAA	ATT	GCT	GCT	AAA	GCT	ATT	GGT	AAA	AAA
	AAC	GAC	AGT	AGA	TAT	CTA	CTT	TAA	CGA	CGA	TTT	CGA	TAA	CCA	TTT	TTT
	Leu	Leu	Ser	Ser	Ile	Asp	Glu	Ile	Ala	Ala	Lys	Ala	Ile	GJA	Lys	Lys>
٠			2	50		2	260			270			28	30		
		•		*	•		•	,	•	*		•		*	•	
	ATA	CAC	CAA	AAT	AAT	GGT	TTG	GAT	ACC	GAA .	TAT	TAA.	CAC	AAT	GGA	TCA
	TAT	GTG U: a	GIT	TTA	TTA	CCA	AAC	CTA	TGG	CIT	ATA	TTA	GTG	TTA	CCT	AGT
	116	nis	GIN	ASII	ASN	GIY	ren	ASD	Tnr	Glu	Tyr	Asn	His	Asn	Gly	Ser>
2	90			300			31	LO		3	20			330		
	•		•	•		•		•	•		•		•	•		•
	TTG	TTA	GCG	GGA	CGT	TAT	GCA	ATA	TCA	ACC	CTA	ATA	AAA	CAA	AAA	TTA
	AAC	AAT	CGC	CCT	GCA	ATA	CGT	TAT	AGT	TGG	GAT	TAT	TTT	GTT	TTT	TAA
	Leu	Leu	AIA	GIĀ	Arg	Тут	Ala	Ile	Ser	Thr	Leu	Ile	Lys	Gln	Lys	ren>
	34	0		3	50			360			37	0		3	80	
		•	•		•		*	•		•		*	•			
	GAT	GGA	TTG	AAA	TAA	GAA	GGA	TTA	AAG	GAA	AAA	TTA	GAT	GCG	GCT	AAG
	LTA	CCT	AAC	TTT	TTA	CTT	CCT	TAA	TTC	CTT	TIT	TAA	CTA	CGC	CGA	TTC
	<b>MSP</b>	erA	rea	Lys	ASD	GIU	GIA	Leu	Lys	Glu	Lys	Ile	Asp	Ala	Ala	Lvs>

#### B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

	390			4 (	00	•		110			420			4:	30
•	*		•		•	•		•		•	•		• ,		•
AAA	TGT	TCT	GAA	ACA	TTT	ACT	TAA	AAA	TTA	AAA	GCA	AAA	CAC	ACA	GAT
					AAA										
Lys	Cys	Ser	Glu	Thr	Phe	Thr	Asn	Lys	Leu	Lys	Ala	Lys	His	Thr	Asp>
	4	140			450			46	50			470			480
•		•		•	•		•		•			•		•	•
CTT	GGT	AAA	GAA	GGT	GTT	ACT	GAT	GCT	GAT	GCA	AAA	GAA	GCC	ATT	TTA
					CAA										
Leu	Gly	Lys	Glu	Gly	Val	Thr	Asp	Ala	Asp	Āla	Lys	Glu	Ala	Ile	Leu>
		49	90		9	500			510			52	20		
	•		•	•	_	•	•	•	•		•		•	•	
AAA	ACA	AAT	GGT	ACT	AAA	ACT	AAA	GGT	GCT	GAA	GAA	CTT	GGA	AAA	TTA
TTT	TGT	TTA	CCA	TGA	TTT	TGA	TTT	CCA	CGA	CTT	CTT	GAA	CCT	TTT	AAT
Ĺys	Thr	Asn	Gly	Thr	Lys	Thr	Lys	Gly	Ala	Glu	Glu	Leu	Gly	Lys	Leu>
530			540			55	50			560			570		
•		• '	•		•		•	. •		•		•	•		•
TTT	GAA	TCA	GTA	GAG	GTC	TTG	TCA	AAA	GCA	GCT	AAA	GAG	ATG	CIT	GCT
AAA	CTT	AGT	CAT	CTC	CAG	AAC	AGT	TTT	CGT	CGA	TTT	CTC	TAC	GAA	CGA
Phe	Glu	Ser	Val	Glu	Val	Leu	Ser	Lys	Ala	Ala	Lys	Glu	Met	Leu	Ala>
5.9	30		,	590			600			61	LO			520	
				220										320	
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	•	GTT		•	CTT	ACA	•	CCT	GTT		•	<b>↓</b> GAA		•	aaa
AAT TTA	TCA AGT	CAA	AAA TTT	GAG CTC	GAA	TGT	AGC TCG	GGA	CAA	GTG CAC	GCA CGT	CTT	AGT TCA	CCA GGT	TIT
AAT TTA	TCA AGT	CAA	AAA TTT	GAG CTC	GAA	TGT	AGC TCG	GGA	CAA	GTG CAC	GCA CGT	CTT	AGT TCA	CCA GGT	
AAT TTA	TCA AGT Ser	CAA	AAA TTT	GAG CTC Glu	GAA Leu	TGT	AGC TCG Ser	GGA Pro	CAA	GTG CAC	GCA CGT Ala	CTT	AGT TCA	CCA GGT Pro	TTT Lys>
AAT TTA	TCA AGT	CAA	AAA TTT	GAG CTC Glu	GAA	TGT	AGC TCG Ser	GGA	CAA	GTG CAC	GCA CGT	CTT	AGT TCA	CCA GGT	TTT Lys>
AAT TTA Asn	TCA AGT Ser	CAA Val	AAA TTT Lys	GAG CTC Glu	GAA Leu 40	TGT Thr	AGC TCG Ser	GGA Pro 550	CAA Val	GTG CAC Val	GCA CGT Ala	CTT Glu	AGT TCA Ser	CCA GGT Pro	TTT Lys>
AAT TTA Asn	TCA AGT Ser 630	CAA Val	AAA TTT Lys CAA	GAG CTC Glu 6	GAA Leu 40	TGT Thr AGC	AGC TCG Ser	GGA Pro 550 *	CAA Val GAC	GTG CAC Val	GCA CGT Ala 660	CTT Glu AAC	AGT TCA Ser	CCA GGT Pro 67	TTT Lys> 10 + TCA
AAT TTA Asn • AAA TTT	TCA AGT Ser 630 CCT GGA	CAA Val AAG TTC	AAA TTT Lys CAA GTT	GAG CTC Glu 64 AAT TTA	GAA Leu 40 • GTT	TGT Thr AGC TCG	AGC TCG Ser AGC TCG	GGA Pro 50 * CTT GAA	CAA Val GAC CTG	GTG CAC Val	GCA CGT Ala 660 AAA TTT	CTT Glu AAC TTG	AGT TCA Ser * AGC TCG	CCA GGT Pro 67 GTT CAA	TTT Lys>  C TCA AGT
AAT TTA Asn • AAA TTT	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC Lys	AAA TTT Lys CAA GTT	GAG CTC Glu 64 AAT TTA	GAA Leu 10 GTT CAA Val	TGT Thr AGC TCG	AGC TCG Ser AGC TCG	GGA Pro 550 * CTT GAA Leu	CAA Val GAC CTG Asp	GTG CAC Val	GCA CGT Ala 660 AAA TTT Lys	CTT Glu AAC TTG Asn	AGT TCA Ser * AGC TCG	CCA GGT Pro 67 GTT CAA	TTT Lys>  C TCA AGT Ser>
AAT TTA Asn • AAA TTT	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC	AAA TTT Lys CAA GTT	GAG CTC Glu 64 AAT TTA	GAA Leu 40 • GTT CAA	TGT Thr AGC TCG	AGC TCG Ser AGC TCG	GGA Pro 550 * CTT GAA Leu	CAA Val GAC CTG	GTG CAC Val	GCA CGT Ala 660 AAA TTT Lys	CTT Glu AAC TTG	AGT TCA Ser * AGC TCG	CCA GGT Pro 67 GTT CAA	TTT Lys>  C TCA AGT
AAT TTA ASD AAA TTT Lys	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC Lys 680	AAA TTT Lys CAA GTT Gln	GAG CTC Glu 6 AAT TTA Asn	GAA Leu 10 GTT CAA Val	TGT Thr AGC TCG Ser	AGC TCG Ser AGC TCG Ser	GGA Pro 550 * CTT GAA Leu	CAA Val GAC CTG Asp	GTG CAC Val GAG CTC Glu	GCA CGT Ala 660 AAA TTT Lys	AAC TTG Asn	AGT TCA Ser AGC TCG Ser	CCA GGT Pro 67 GTT CAA Val	TIT Lys> 0 * TCA AGT Ser>
AAT TTA ASD AAA TTT Lys	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC Lys 680	AAA TTT Lys CAA GTT Gln	GAG CTC Glu 6 AAT TTA Asn	GAA Leu 10 GTT CAA Val 690	TGT Thr AGC TCG Ser	AGC TCG Ser AGC TCG Ser	GGA Pro 550 CTT GAA Leu 70	GAC CTG Asp	GTG CAC Val GAG CTC Glu	GCA CGT Ala 660 AAA TTT Lys	AAC TTG ASD	AGT TCA Ser * AGC TCG Ser	CCA GGT Pro 67 GTT CAA Val	TIT Lys> 0 * TCA AGT Ser>
AAT TTA ASD AAA TTT Lys GTA CAT	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC Lys 680 TTG AAC	AAA TTT Lys CAA GTT Gln CCT GGA	GAG CTC Glu 6. AAT TTA ASN	GAA Leu 10 GTT CAA Val 690 GAA CTT	TGT Thr AGC TCG Ser ATG TAC	AGC TCG Ser AGC TCG Ser AAA TTT	GGA Pro 50 * CTT GAA Leu 70 GTT CAA	GAC CTG Asp	GTG CAC Val GAG CTC Glu GTA CAT	GCA CGT Ala 660 AAA TTT Lys AGC TCG	AAC TTG ASD 710 AAA TTT	AGT TCA Ser AGC TCG Ser GAA CTT	CCA GGT Pro 67 GTT CAA Val	TIT Lys> 0 * TCA AGT Ser> 720 * AAC
AAT TTA ASD AAA TTT Lys GTA CAT	TCA AGT Ser 630 CCT GGA Pro	AAG TTC Lys 680 TTG AAC Leu	AAA TTT Lys CAA GTT Gln CCT GGA	GAG CTC Glu 6. AAT TTA ASN	GAA Leu 10 GTT CAA Val 690 GAA CTT Glu	TGT Thr AGC TCG Ser ATG TAC	AGC TCG Ser AGC TCG Ser AAA TTT	GGA Pro 50 * CTT GAA Leu 70 GTT CAA	GAC CTG Asp	GTG CAC Val GAG CTC Glu GTA CAT	GCA CGT Ala 660 AAA TTT Lys AGC TCG	AAC TTG ASD 710 AAA TTT Lys	AGT TCA Ser AGC TCG Ser GAA CTT Glu	CCA GGT Pro 67 GTT CAA Val	TIT Lys> 0 + TCA AGT Ser> 720 + AAC
AAT TTA ASD AAA TTT Lys GTA CAT	TCA AGT Ser 630 CCT GGA Pro	AAG TTC Lys 680 TTG AAC Leu	AAA TTT Lys CAA GTT Gln CCT GGA Pro	GAG CTC Glu 6. AAT TTA ASN	GAA Leu 10 GTT CAA Val 690 GAA CTT Glu	TGT Thr AGC TCG Ser ATG TAC Met	AGC TCG Ser AGC TCG Ser AAA TTT	GGA Pro 50 * CTT GAA Leu 70 GTT CAA	GAC CTG Asp CTT GAA Leu	GTG CAC Val GAG CTC Glu GTA CAT	GCA CGT Ala 660 AAA TTT Lys AGC TCG	AAC TTG ASD 710 AAA TTT Lys	AGT TCA Ser AGC TCG Ser GAA CTT	CCA GGT Pro 67 GTT CAA Val	TIT Lys> 0 + TCA AGT Ser> 720 + AAC
AAT TTA ASD AAA TTT Lys GTA CAT Val	TCA AGT Ser 630 CCT GGA Pro GAT CTA ASP	CAA Val AAG TTC Lys 680 TTG AAC Leu 7	AAA TTT Lys CAA GTT Gln CCT GGA Pro	GAG CTC Glu 6 AAT TTA ASN GGT CCA Gly	GAA Leu  O GTT CAA Val  690 GAA CTT Glu  GAT	TGT Thr AGC TCG Ser ATG TAC Met	AGC TCG Ser AGC TCG Ser AAA TTT Lys	GGA Pro 550 CTT GAA Leu 70 GTT CAA Val	GAC CTG Asp CTT GAA Leu 750	GTG CAC Val GAG CTC Glu GTA CAT Val	GCA CGT Ala 660 AAA TTT Lys AGC TCG Ser	AAC TTG ASD 710 AAA TTT Lys 70	AGT TCA Ser * AGC TCG Ser GAA CTT Glu	CCA GGT Pro 67 GTT CAA Val AAA TTT Lys	TIT Lys> 0 * TCA AGT Ser> 720 * AAC TTG Asn>
AAT TTA ASD AAA TTT Lys GTA CAT Val	TCA AGT Ser 630 CCT GGA Pro GAT CTA ASP	AAG TTC Lys 680 TTG AAC Leu 7 GGC CCG	AAA TTT Lys CAA GTT GIn CCT GGA Pro 30 AAG TTC	GAG CTC Glu 6 AAT TTA ASN GGT CCA Gly TAC ATG	GAA Leu  10 GTT CAA Val  690 GAA CTT Glu  GAT CTA	TGT Thr AGC TCG Ser ATG TAC Met 740 CTA GAT	AGC TCG Ser AGC TCG Ser AAA TTT Lys	GGA Pro 550 * CTT GAA Leu 70 GTT CAA Val	GAC CTG ASP CTT GAA Leu 750 ACA	GTG CAC Val GAG CTC Glu GTA CAT Val	GCA CGT Ala 660 AAA TTT Lys AGC TCG Ser	AAC TTG ASD TTT LYS AAG TTC	AGT TCA Ser * AGC TCG Ser GAA CTT Glu	CCA GGT Pro 67 GTT CAA Val AAA TTT Lys	TIT Lys> 0 * TCA AGT Ser> 720 * AAC TTG ASD>
AAT TTA ASD AAA TTT Lys GTA CAT Val	TCA AGT Ser 630 CCT GGA Pro GAT CTA ASP	AAG TTC Lys 680 TTG AAC Leu 7 GGC CCG	AAA TTT Lys CAA GTT GIn CCT GGA Pro 30 AAG TTC	GAG CTC Glu 6 AAT TTA ASN GGT CCA Gly TAC ATG	GAA Leu  10 GTT CAA Val  690 GAA CTT Glu  GAT CTA	TGT Thr AGC TCG Ser ATG TAC Met 740 CTA GAT	AGC TCG Ser AGC TCG Ser AAA TTT Lys	GGA Pro 550 * CTT GAA Leu 70 GTT CAA Val	GAC CTG ASP CTT GAA Leu 750 ACA	GTG CAC Val GAG CTC Glu GTA CAT Val	GCA CGT Ala 660 AAA TTT Lys AGC TCG Ser	AAC TTG ASD TTT LYS AAG TTC	AGT TCA Ser * AGC TCG Ser GAA CTT Glu	CCA GGT Pro 67 GTT CAA Val AAA TTT Lys	TIT Lys> 0 * TCA AGT Ser> 720 * AAC TTG Asn>

#### B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

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															CCG	
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															CTA	
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	Lys	Ala	Asp	Lys	Ser	Lys	Val	Lys	Leu	Thr	Ile	Ser	Asp	Asp.	Leu	Gly>
	-	870			88	30 -		ε	390			900			9;	.0
	•	*		•		•	•		•		•	•		•		•
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	Gln	Thr	Thr	Leu	Glu	Val	Phe	Lys	Glu	Asp	GJA	Lys	Thr	Leu	Val	Ser>
		9	920			930			94	10		9	950			960
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٠ ـ ٠	TTT	TTT	CAT	TGA	AGG	TTT	CTG	TTC	AGT	AGT	TGT	CTT	CTT	TTT	AAG	TTA
	Lys	Lys	Val	Thr	Ser	Lys	Asp	Lys	Ser	Ser	Thr	Glu	Glu	Lys	Phe	Asn>
	•		97	70		9	980		•	9 <b>9</b> 0			100	00		
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	CTT	TTT	CCA	CTT	CAT	AGA	CTT	TTT	TAT	TAT	TGT	TCT	CGT	CTG	CCT	TGG
	Glu	Lys	Gly	Glu	Val	Ser	Glu	Lys	Ile	Ile	Thr	Arg	Ala	Asp	Gly	Thr>
10	10			1020			10:	30		1	040		3	1050		
	•		•	•		•		•	•		•		•			•
	AGA	CTT	GAA	TAC	ACA	GGA	ATT	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCT	AAA
٠															'CGA	
	Arg	Leu	Glu	Tyr	Thr	Gly	Ile	Lys	Ser	Asp	Gly	Ser	Gly	Lys	Ala	Lys>
	10	60		1	070		:	1080			109	90		1:	100	
		•	•		◆.		•	•		•		•	•		*	
	GAG	GTT	TTA	AAA	GGC	TAT	GTT	CTT	GAA	GGA	ACT	CTA	ACT	GCT	GAA	AAA
																TTT
	Glu	Val	Leu	Lys	Gly	Tyr	Val	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys>
		1110			11.	20		1	130			1140			11	50
	•	•		•		•	•		•		•	•		•		•
	ACA	ACA	TTG	GTG	GTT	AAA	GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	ATT
	TGT	TGT	AAC	CAC	CAA	TTT	CTT	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	AAT
	77 h	The		37 - 1	Mal.	Tare	G1.,	C3.4	The	17= 1	The	Tan	50-	1110	1	Ile>

FIGURE 31 (3 of 4)

B-31 OSP C/ B-31 OSP A / B-31 OSP B FUSION

1160 1170 1180 1190 1200

TCA AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT AGT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA Ser Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser>

1210 1220 1230 1240

GCT GCT ACT AAA AAA ACT GCA GCT TGG AAT GAC AGT ACT AGC ACT TTA CGA CGA TGA TTT TTT TGA CGT CGA ACC TTA CTG TCA TGA TCG TGA AAT Ala Ala Thr Lys Lys Thr Ala Ala Trp Asn Asp Ser Thr Ser Thr Leu>

1250 1260 1270 1260 1290

ACA ATT AGT GCT GAC AGC AAA AAA ACT AAA GAT TTG GTG TTC TTA ACA TGT TAA TCA CGA CTG TCG TTT TTT TGA TTT CTA AAC CAC AAG AAT TGT Thr Ile Ser Ala Asp Ser Lys Lys Thr Lys Asp Leu Val Phe Leu Thr>

1300 1310 1320 1330 1340

GAT GGT ACA ATT ACA GTA CAA CAA TAC AAC ACA GCT GGA ACC AGC CTA CTA CCA TGT TAA TGT CAT GTT GTT ATG TTG TGT CGA CCT TGG TCG GAT ASP Gly Thr Ile Thr Val Gln Gln Tyr Asn Thr Ala Gly Thr Ser Leu>

1350 1360 1370 1380 1390

GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT TCA GAG CTT AAA AAC GCT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA AGT CTC GAA TTT TTG CGA Glu Gly Ser Ala Ser Glu Ile Lys Asn Leu Ser Glu Leu Lys Asn Ala>

1400

TTA AAA TAA AAT TTT ATT Leu Lys ***>

FIGURE 31 (4 of 4)

#### FUSION SEQUENCE

B-31 OSP A/ B-31 P-93 (1168-2100) Sequence Range: 1 to 1720

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77	10 C	AA TT	AAT	Car	r ag Mac	C AG	C CI	T GA	C G	AG	AAA	AA A	C AC	C G	T T	CA	GTA	GAT
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	100				110			12				:	130			14	0	
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CC	CAA	1G. 1	TAC	GAT	CTA	ATI	GCX	AC	A GT	Ά .	GAC	AAC	CT.	r ga	G CI	T A	AA	GGA
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	15	0			1	60			170				180	)			19	0
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TG	A AG	A C	TA	AAA TTT	AAC	AAT	GGA	TCI	GG	<b>λ</b> (	GTA	CTT	GAA	GGC	GT	A A	4.A	GCT
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GAC	. AA	A A	- GT	444	CTA	* * * * * * * * * * * * * * * * * * * *		•		•		•				•		
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ACA	CTI	. G	AA (	STT	TTC	AAA	CAA	ChT	CCC		•		•		*		•	
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GTA	ACT	T	CC A	LAA	GAC	AAG	TCA	TCD	אכא	G	<b>a</b> a c	* 7. 7.			•			*
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B-31 OSP A/ B-31 P93

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GAA	TAC	ACA	GGA	ATT	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCT	AAA	GAG	GTT
														CIC	
E	Y	4.	G	I	K	5	ע	G	S	G	K	A	.K	E	V>
-		440			450			4	60			470			480
		•		•	•		•		•	. •		•		•	400
TTA	AAA	GGC	TAT	GTT	CTT	GAA	GGA	ACT	CTA	ACT	GCT	GAA	AAA	ACA	ACA
TAA	TTT	CCG	ATA	CAA	GAA	CIT	CCI	TGA	GAT	TGA	CGA	CII	TTT	TGT	TGT
L	K	G	Y	V	L	E	G	T	L.	T -	<del>1</del>	E	K	T	T>
		4	90			500			510			ς.	20		
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TTG	GTG	GTT	AAA	GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	ATT	TCA	AAA
			TTT	CTT	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	TAA	AGT	TTT
L	V	V	K	E	G	T	V	T	L	S	K	N	I	S	K>
530			540			5	50		1	560			570		
*		*	•		•			•				•	370		•
TCT	GGG	GAA	GTT	TCA	GTT	GAA	CTT	AAT	GAC	ACT	GAC	AGT	AGT	GCT	GCT
												TCA	TCA	CGA	CGA
S	G	· E	v	s	V.	E	L	N	D	T	D	S	S	A	A>
58	80		9	590			600			61	מו			:20	
-	80	•	5	590		•	600		•	61	10	*	. (	520	
ACT	AAA	• AAA	ACT	GCA	GCT	• TGG	• Taa	TCA	GGC	ACT	+ TCA	* ACT	TTA	ACA	ATT
ACT TGA	AAA TTT	TTT	ACT TGA	GCA CGT	CGA	ACC	• TAA TTA	AGT	GGC CCG	ACT TGA	+ TCA	ACT TGA	TTA	•	ATT TAA
ACT TGA	AAA TTT	TTT	ACT TGA	GCA CGT	GCT CGA A	ACC	• TAA TTA	AGT	GGC CCG	ACT TGA	+ TCA	ACT TGA T	TTA	ACA	ATT TAA I>
ACT TGA	AAA TTT	TTT	ACT TGA	GCA CGT A	CGA	ACC	AAT TTA N	AGT	GGC CCG	ACT TGA	TCA AGT S	TGA	TTA AAT	ACA TGT T	TAA I>
ACT TGA T	AAA TTT K	TTT K	ACT TGA T	GCA CGT A	CGA A	ACC W	AAT TTA N	AGT S	GGC CCG G	ACT TGA T	TCA AGT S	TGA T	TTA AAT L	ACA TGT T	TAA I>
ACT TGA T	AAA TTT K 630 GTA	TTT K AAC	ACT TGA T	GCA CGT A 64	CGA A 10 AAA	ACC W ACT	AAT TTA N	AGT S 50 GAC	GGC G G	ACT TGA T	TCA AGT S 660	TGA T	TTA AAT L	ACA TGT T	TAA I> 0
ACT TGA T ACT TGA	AAA TTT K 630 GTA CAT	TTT K AAC TTG	ACT TGA T AGT TCA	GCA CGT A 64 AAA TTT	CGA A 10 AAA TTT	ACC W ACT TGA	AAT TTA N	AGT S 550 GAC CTG	GGC CCG G	ACT TGA T GTG CAC	TCA AGT S 660 TTT	TGA T ACA TGT	TTA AAT L AAA TTT	ACA TGT T 67 GAA CTT	TAA I> 0 AAC TTG
ACT TGA T ACT TGA	AAA TTT K 630 GTA CAT	TTT K AAC TTG	ACT TGA T AGT TCA	GCA CGT A 64 AAA TTT	CGA A 10 AAA TTT	ACC W ACT TGA	AAT TTA N	AGT S 550 GAC CTG	GGC CCG G	ACT TGA T GTG CAC	TCA AGT S 660 TTT	TGA T ACA TGT	TTA AAT L AAA TTT	ACA TGT T	TAA I> 0 AAC TTG
ACT TGA T ACT TGA	AAA TTT K 630 GTA CAT V	TTT K AAC TTG	ACT TGA T AGT TCA	GCA CGT A 64 AAA TTT	CGA A 10 AAA TTT	ACC W ACT TGA	AAT TTA N	AGT S 550 GAC CTG	GGC CCG G CTT GAA L	ACT TGA T GTG CAC	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T	TTA AAT L AAA TTT	ACA TGT T 67 GAA CTT	TAA I> O AAC TTG 'N>
ACT TGA T ACT TGA T	AAA TTT K 630 GTA CAT V	AAC TTG N	ACT TGA T AGT TCA S	GCA CGT A 64 AAA TTT K	CGA A 10 AAA TTT K 690	ACC W ACT TGA	AAT TTA N AAA TTT K	AGT S S S GAC CTG D 70	GGC CCG G CTT GAA L	ACT TGA T GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T	TTA AAT L * AAA TTT K	ACA TGT T 67 GAA CTT E	TAA I>  O AAC TTG N> 720
ACT TGA T ACT TGA T	AAA TTT K 630 GTA CAT V	AAC TTG N 580	ACT TGA T AGT TCA S	GCA CGT A 64 AAA TTT K	CGA A 10 AAA TTT K 690 CAA	ACC W ACT TGA .T.	AAT TTA N AAA TTT K	AGT S S S GAC CTG D 70 TCA	GGC CCG G CTT GAA L.	ACT TGA T + GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T	TTA AAT L AAA TTT K	ACA TGT T 67 GAA CTT E	TAA I>  O AAC TTG 720
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ACT TGA T ACT TGA T ACA TGT	AAA TTT K 630 GTA CAT V	AAC TTG N 580 ACA TGT	ACT TGA T AGT TCA S GTA CAT	GCA CGT A 64 AAA TTT K	CGA A 10 AAA TTT K 690 CAA GTT	ACC W ACT TGA TAC ATG	AAA TTTA N AAA TTT K GAC CTG	AGT S S S GAC CTG D TCA AGT	GGC CCG G CTT GAA L	ACT TGA T GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T	TTA AAT L AAA TTT K TTA AAT	ACA TGT T 67 GAA CTT E	TAA I>  0 AAC TTG N>  720 GGG CCC
ACT TGA T ACT TGA T ACA TGT	AAA TTT K 630 GTA CAT V	AAC TTG N 580 ACA TGT T	ACT TGA T AGT TCA S GTA CAT	GCA CGT A 64 AAA TTT K	CGA A 10 AAA TTT K 690 CAA GTT Q	ACC W ACT TGA TAC ATG	AAT TTA N AAA TTT K GAC CTG D	AGT S S S GAC CTG D TCA AGT	GGC CCG G CTT GAA L	ACT TGA T GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T 10 AAA TTT K	TTA AAT L AAA TTT K TTA AAT L	ACA TGT T 67 GAA CTT E	TAA I>  0 AAC TTG N>  720 GGG CCC
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ACT TGA T ACT TGA T ACA TGT T	AAA TTT K 630 GTA CAT V ATT TAA I	AAC TTG N 580 ACA TGT T 7:	ACT TGA T AGT TCA S GTA CAT V	GCA CGT A 64 AAA TTT K CAA GTT Q	CGA A 10 AAA TTT K 690 CAA GTT Q	ACT TGA TAC ATG Y	AAA TTTA N AAA TTT K GAC CTG D	AGT S GAC CTG D 70 TCA AGT S GAT	GGC CCG G CTT GAA L O AAT TTA N 750	ACT TGA T GTG CAC V GGC CCG G	TCA AGT S 660 TTT AAA F ACC TGG T	TGA T ACA TGT T AAA TTT K AAC	TTA AAT L AAA TTT K TTA AAT L	ACA TGT T 67 GAA CTT E GAG CTC E	TAA I> 0 AAC TTG N> 720 GGG CCC G>
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FIGURE 32 (2 of 5)

B-31 OSP A/ B-31 P-93

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B-31 OSP / B-31 P-93

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	CAG GTC Q ATG	CGG GCC R 1	ATA Y 400 TCA AGT S	GGA CCT G	ATT TAA I AAA TTT K	TAT ATA Y 1410 GCT CGA A	GAA CTT E AAG TTC K	CGT GCA R CTT GAA L	GAA CTT E 14: CAG GTC Q	AAA TTT K 20 ATA TAT	GAT CTA D CTT GAA L	TTG AAC L 10 GAT CTA	GTT CAA V 130 AAA TTT	GTT CAA V CTT GAA L	ATT TAA I GAA CTT	AAA TTT K> 1440 AAT
	CAG GTC Q ATG TAC	CGG GCC R 1. GAT CTA D	ATA Y 400 TCA AGT S	GGA CCT G GGA CCT G	ATT TAA I AAA TTT K	TAT ATA Y 1410 GCT CGA A	GAA CTT E AAG TTC K	CGT GCA R CTT GAA L	GAA CTT E 14: CAG GTC Q	AAA TTT K 20 ATA TAT I	GAT CTA D CTT GAA L	TTG AAC L 14 GAT CTA D	GTT CAA V 130 AAA TTT K	CTT GAA L	ATT TAA I GAA CTT E	AAA TTT K> 144C AAT TTA N>
	CAG GTC Q ATG TAC M	CGG GCC R 1. GAT CTA D	ATA Y 400 TCA AGT S 14 GTG	GGA CCT G GGA CCT G	ATT TAA I AAA TTT K	TAT ATA Y 1410 GCT CGA A	GAA CTT E AAG TTC K	CGT GCA R CTT GAA L	GAA CTT E 14: CAG GTC Q	AAA TTT K 20 ATA TAT I 1470	GAT CTA D CTT GAA L	TTG AAC L 14 GAT CTA D AAT	GTT CAA V 130 AAA TTT K	CTT CAA V CTT GAA L	ATT TAA I GAA CTT E	AAA TTT K> 1440 AAT TTA N>
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	CAG GTC Q ATG TAC M TTA AAT L	CGG GCC R I GAT CTA D AAX TTT K	ATA Y 400 TCA AGT S 14 GTG CAC V	GGA CCT G GGA CCT G SO GTA CAT V	ATT TAA I AAA TTT K TCA AGT S	TAT ATA Y 410 GCT CGA A 1 GAG CTC	GAA CTT E AAG TTC K 460 TCT AGA S	CGT GCA R CTT GAA L AAT TTA N	GAA CTT E 14: CAG GTC Q TTT AAA F	AAA TTT K 20 ATA TAT I 1470 GAG CTC E	GAT CTA D CTT GAA L ATT TAA I	TTG AAC L GAT CTA D AAT TTA	GTT CAA V 130 AAA TTT K 141 AAA TTT K	CTT GAA L SO AAT TTA N 1530	ATT TAA I GAA CTT E TCA AGT S	AAA TTT K> 144C AAT TTA N> TCT AGA S>
	CAG GTC Q ATG TAC M TTA AAT L 490 CTT	CGG GCC R I GAT CTA D AAÄ TTT K	ATA Y 400 TCA AGT S 14 GTG CAC V	GGA CCT G GGA CCT G TA CAT V	ATT TAA I AAA TTT K TCA AGT S	TATA Y 410 GCT CGA A 1 GAG CTC E	GAA CTT E AAG TTC K 460 TCT AGA S 15	CGT GCA R CTT GAA L AAT TTA N	GAA CTT E 14: CAG GTC Q TTT AAA F	AAA TTT K 20 ATA TAT I 1470 GAG CTC E 1	GAT CTA D CTT GAA L ATT TAA I 520 GCT	TTG AAC L 10 GAT CTA D AAT TTA N GTT	GTT CAA V 130 AAA TTT K 141 AAA TTT K	CTT CAA V CTT GAA L 30 AAT TTA N 1530 GAT	ATT TAA I GAA CTT E TCA AGT S	AAA TTT K> 144C AAT TTA N> TCT AGA S>
1	CAG GTC Q ATG TAC M TTA AAT L 490 CTT GAA	CGG GCC R I GAT CTA D AAA TTT K	ATA Y 400 TCA AGT S 14 GTG CAC V	GGA CCT G GGA CCT G GTA CAT V 1500	ATT TAA I AAA TTT K TCA AGT S	TATA Y 410 GCT CGA A 1 GAG CTC E AAA TTT	GAA CTT E AAG TTC K 460 TCT AGA S 15	CGT GCA R CTT GAA L AAT TTA N	GAA CTT E 14: CAG GTC Q TTT AAA F	AAA TTT K 20 ATA TAT I 1470 GAG CTC E 1 GTA CAT	GAT CTA D CTT GAA L ATT TAA I S20 CCT CGA	TTG AAC L 14 GAT CTA D AAT TTA N GTT CAA	GTT CAA V 130 AAA TTT K 141 AAA TTT K	CTT CAA V CTT GAA L 30 N 1530 GAT CTA	ATT TAA I GAA CTT E TCA AGT S AAA TTT	AAA TTT K> 144C AAT TTA N> TCT AGA S>

B-31 OSP A/ B-31 P-93

1550 1560 1570 AGT AGT AAT GAT TGG AGA TTG GCC AAA TTT TCT CCT AAA AAT TTA GAT TCA TCA TTA CTA ACC TCT AAC CGG TTT AAA AGA GGA TTT TTA AAT CTA S S N D W R L A K F S P K N L D> 1600 1590 1610 1620 GAG TTT ATT CTT TCA GAG AAT AAA ATT ATG CCT TTT ACT AGC TTT TCT CTC AAA TAA GAA AGT CTC TTA TTT TAA TAC GGA AAA TGA TCG AAA AGA EFILSENKIMPFTSFS> 1640 1650 1660 1670 • GTG AGA AAA AAT TTT ATT TAT TTG CAA GAT GAG TTT AAA AGT CTA GTT CAC TCT TTT TTA AAA TAA ATA AAC GTT CTA CTC AAA TTT TCA GAT CAA V R K N F I Y L Q D E F K S L V> 1690 1700 1710 ATT TTA GAT GTA AAT ACT TTA AAA AAA GTT AAG GGT CAC C TAA AAT CTA CAT TTA TGA AAT TTT TTT CAA TTC CCA GTG G I L D V N T L K K V K G H X>

FIGURE. 32 (5 of 5)

B-31 OSP B/ B-31 P41 (122-234)

OSPB/Fla122-234

Sequence Range: 1 to 1180

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# B-31 OSP B/ B-31 P41 (122-234)

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	CT	7 C	CT.	TCL	CTT	GT CA	A G	rc c	GGA	AAA	AC.	A A	CA (	GTG	GAA	AT	TA	AA d	22.2		_
	E			100	GAA t	CA V	T C	iG (	CT	TTT	TG	T T	GT (	CAC	CIT	TA	A T	TT C	المرارة م	, 66	<b>7</b>
			_	_	ב	v	'	′	G ,	K	T	•	r	v	E	I	1	ĸ	E	G	^ >
7.2. 3		580				590				600										Ū	
		*		•		•		•						61	_			62			
	AC:	G	TT :	ACT	CTA	AAJ	A AG	A G			GAZ				•		•		•		
	TG	C	AA 1	TGA	GAT	TTT	TC	TC	TT 7	AA1	CTT	, 444 , 357	ντ c	AT (	JGA	AAZ	7 G1	A A	AA	GT	2
	T		V	T.	L.	K	R		E	I	Ε	K		ם זער ר	-C1	11.1	CA	T T	TT	CAC	3
												-		•	J	v	V	<b>'</b>	K	V:	•
	*	ъ.	30		_	6	40			6	50			6	60				-ء		
	TTT	مله	רה ז	) T	- <b>.</b>		*	_	•		•		•				•		67		
	AAA	ΑZ	AC T	ידא ידא	CTC	ACT	GC	A GO	GT T	'CT	AAC	AA	A A	AA A	CA (	GT	AA	A TY	300	GAZ	
	F	I	, .	N	D	TGA T	, CG	r co	⊒A A •	GA '	TIG	TT	TT	lt t	GT (	CA	TT	TAC	20	CTT	
				• • • • • • • • • • • • • • • • • • • •		T	^	٠.	۰	S	N	K	. }	ζ '	T	G	K	F	V	E>	
			68	0			690	)				20			_						
	•			•		•		,		•		00			71					720	
(	GAC	AG	TA	CT 1	AGC	ACT TGA	TT	AC	A A	TT I	AGT	GC	מס יו	- 	~~ .	•				•	
•	CIG	TC	AT	GA 7	rcg	TGA T	AAT	TG	TT	AA 7	rca	CG	CT	C A	3C A	AA	AA	A AC	T.	AAA	
	ט	S	,	T	S	T	L	T	• :	I	s	A	D		-G 1 S	* 1	TT	TG	A '	TTT	
				77-	·									•	<del>-</del> .	••	v	T		K>	
		•		730		٠.		740				750	)			76	50				
C	TAE	TT	G G	יים. דיים דיים	· •	ت الدران ع		•	_	•	,	•		•	•				•		
Ċ	TA	AA		AC A	AC.	ATT AAT	ACA	GA	T GC	A TE	CA	ATI	' AC	A GI	A C	AΑ	CAA	TA	; ۲	AC	
	D	L	٠,	,	F	AAT L	T G T	CT				***	. 10	1 6	11 G	TT	GTT	, Бал	C 5	~~~	
					•		1	ט	G	;	T	·I	T	ν	,	0	0	v	•	NI.	

FIGURE 33 (2 of 4)

# B-31 OSP B/ B-31 P41 (122-234)

	770			780	)		7	790			800			816	,	
	•		•		r	•		•	•	•	•		•			
	ACA	CC	r GGA	ACC	AGC	CTA	GAZ	A GGA	TCA	GC#	AG:	GA)	AT:	נגג ז	AA	r cii
	TGT	CGX	CCI	TGG	TCG	GAT	CII	CCT	' AG7	CGI	TC	CTT	LAT 7	TT	TT	623
	T	A	G	T	S	· L	E	G	S	A	S	· E	I	K	N	L>
		20			1											
	0	20			830		•	840				350			860	
	TCA		لىلىل.			- CCT		•		. •		•	•		•	
	AGT	CTC	GAA	TTT	י שער י	CCA	774	. WAYA	CCA	CAC	CCC	ATG	GCI	, CYS	TAT	AAC TTG
	s	E	L	K	N	A	T.	K	CCA	. u.	D-	TAC	CGA	GTI	' ATA	TTG N>
						••		••	·	44.5		m	A	Q	Y	N>
		870			8	80			890			900			9	10
	*	•		•		•	•		•		•	*		•		_
	CAA	ATG	CAC	ATG	TTA	TCA	AAC	AAA	TCT	GCT	TCT	CAA	AAT	GTA	AGA	ACA
	611	IAC	010	IMC	AAT	AGT	TTG	TTT	AGA	CGA	AGA	CTT	T that	CAT	T	-
	Q	М	H	М	L	S	. <b>N</b>	K	S	A	S	Q	N	V	R	T>
			920			930				4.0						
	•		*		٠	930		•	9	40			950			960
	GCT	GAA	GAG	CTT	GGA	ATG	CAG	CCT	GCA	444	Σ <del>ተ</del> ስተ	220	A C A		•	TCA
	CGA	CTT	CTC	GAA	CCT	TAC	GTC	GGA	CGT	TTT	TAA	TTG	TCT	CCA	GCA	TCA
	A	E	E	Ĺ	G	M	Q	P	A	ĸ	I	N	T	D D	A	AGT
													_	•	^	3,
		•	9	70	_	:	980			990			10	00		
	СТТ	TCL	ccc	ماستات -	C	~~~		-	•			*		•	•	*
	GAA	AGT	CCC	CII	CTT	CCC	1CT	TGG	ACT	TTA	AGA	GTT	CAT	GTT	GGA	GCA
	L	s	G	L	0	A	AGA S	ACC W	1GA	AAT	TCT	CAA	GTA			
				_	•	••	J	**				v	H	V	G	A>
1	010 -			1020			103	30	•	10	40		•	1050		
	•	_	•	•		•		*	•		•		•			
	ACC	CAA	GAT	GAA	GCT	ATT	GCT	GTA	AAT	TTA	TAT	GCA	GCT	AAT	GTT	GCA
	T	G11	D	C11	CGA	TAA	CGA	CAT	TTA	TAA	ATA	CGT	CGA	TTA	CAA	CGT
	•	v	U	E	A	1	A	v	N	I	Y	A	A	N	v	A>
	106	50		10	70		1	.080			109					
			•		•		•	•				•			.00	
	AAT	CTT	TTC	TCT	GGT	GAG	GGA	CCT.	CAA	ACT	GCT	CAG	CCT	GC A	CCC.	
			1270	AUA				I CLA	- crawin	ALC 2	~~ `	~~~	~~~			
	N	L	F	S	G	E	G	A	Q.	T	A	Q	A	A	P	CAA V>
		110														•
	•			•	112	ų.	•	11	30		. 1	140			115	-
	CAA	GAG	GGT	GTT	CAA	CAG		GGA		C3.	~	•		•		•
	GTT	CTC	CCA	CAA	GTT	GTC	CLL	CCT	CC7 GC1	CAA CTT	CAG	CCA	GCA	CCT	GCT	ACA
	Q	E	G	v	Q	Q	E	G	A	Q	910	D 1	CGT A	GGY D	CGA	TGT
						-		-		_	~	_	-	_		1.

B-31 OSP B/ B-31 P41 (122-234)

GCA CCT TCT CAA GGC GGA GTT GGT CAC C
CGT GGA AGA GTT CCG CCT CAA CCA GTG G
A P S Q G G V G H X>

FIGURE 33 (4 of 4)

B-31 OSP B / B-31 P41 (122-295)

Sequence Range: 1 to 1363

20 30 10 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT S I G S Q K E N D L> AQKGAE 50 60 70 80 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA-AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 100 110 120 130 140 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT ARA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 150 160 170 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 210 200 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA I D Q V E L K G T S D K N N> 250 260 270 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 290 300 310 320 . • TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 350 340 360 . 370 380 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT N Q K I S S K V T K K Q G S>

FIGURE 34 (1 of 4)

# B-31 OSP B / B-31 P41 (122-295)

			39	0				400					410				4	20					
	•					*		•		, •	•		_										130
	A	ATA	ACA	A GA	AG (	SAA	AC TG	TC	TC	AAA	G	CT	AA'	TA	AA	TT	λG	AC	TC	'A &	, AC	887	~
	1	I	T G	ر با د د 1		TT.	TG.	A G	AG	TTI	· C	GA	TT	A T	TT	AA	T C	TG	AG	TI	TC	TTT	
		-	•	•	•		T	•	L	K		A	N		K	L		D	S		K	ĸ	L
٠.				440				4					•	160									
•		*		•			•		•			•					•		70				48
	A(	CA CT	AGA	TC	A A	AC	GGZ	A	T.	ACA	CI	T	GAA	T	AC '	TC	C	<b>A</b> A	ATA	A A	, אנה	י הארב	~~
	1	r	R	S	1 1	N N	CCI	TC	A '	TGT	GA	LA ·	CTI	` A'	TG:	AGI	G	LT	TAT	T	GT (	TA	CG
			••	Ū		44	G	. 1		T	L		E	3	Y	S	C	5	I	•	r	D	A:
					490				² 5 (					51									
	Ć.			-	•					•		,	_							20			
	CT	ים י	ዲዲፕ ፖጥአ	GC	T A	CA.	AAA TTT	GC	A C	TA	GA	A A	CI	CI	CA A	AA	AA	T	AGC	A7	T 1	24	املت
	D	,	N	A	4 16	L ⊃1	TTT K	CG	T C	AT	CI	T 7	rga –	GΑ	T	LTŢ	TT	Ά :	rcg	TA	AT	TC	GAA
				-		•	K	^		V	ב		T	L	•	K	N		S	I		K	Ĺ>
	530				54	0	•			55	0				56	0				c <b>~</b>		•	
	G N	<b>.</b> .				•		•			•		•					•		57	-		
	CT	TO	CT	TCA	C.I	T (	GTA CAT	GT	G	GA	AA	A A	CA	AC.	A G	TG	GA	A A	TT	AA	A G	AA (	GGT.
	E		G	S	L		CAT	UAC	⊃ د	CT	TTI	T	GT.	TG	TC	AC	CT.	T	AA	TT'	r c	TT (	CCA
							v	•	,	G	r	٠	1	T		V	Ε		I	K	Ε	:	G>
	5	580	)	_		59	0			.1	600	)				61	0				620		
	ACT	r G	ТТ	ው ጉጋል	СТ	B B	* * * * * * * * * * * * * * * * * * * *		•		•			٠					•				
	TGA	C	AA	TGA	GA'	a a	AA TT K	TOT	. G/	AA A	ATT	. G	AA To	AAZ	A GZ	4T	GGA	A	A.A	GT?	AA	A C	STC
	T		v	T.	L		ĸ	R	E		I		F. I.	א הנהנ	ני כי	ra `	CCT	T:	TT .	CAT	TT.	T C	AG
		-									-	•		Λ.	L		G		K	V	K		V>
	•	ъ.	30				64	0				650					660					670	
	TTT	T	rg 2	AAT	GAY	<b>.</b> .	Ст ,	T CCN		*		•			•		•			•		•	
	TTT AAA F	A	AC 2	ATT	CTO	T	GA (	CGT	CC	1 1	CT	AA Total	C Y	AAA	AA	A	ACA	GG	T A	AAA	TG	3 G	AA
	F.	I	<u>.</u>	N,	Ď	7	r	À	G		S	. · · N	. G	K	TT	T ?	rgt	CC	A :	LTI	ACC	: C	TT
															•		1		•	K	W		E>
			68	*		•	•	590			_		700				7	710				7	20
•	GAC	AG	T A	CT	AGC	ÀC	י ד	TA	20	<b>8</b> 8	<b>₽</b>	3.0	• •			*		•			•		•
0	GAC CTG D	TO	A T	ĠΆ	TCG	TG	A A	LAT	TG'	TT	AA	TC	A C	CT	GA(	CA	GC	AA	A A	AA	ACI	` A.	AA
	D	S	;	T ,	S	T		L.	T		I	s		A	D	1 د	S	J.L.	TT	TT	TGA	. T	T
										-					i		_	А		v	T	3	<b>&lt;&gt;</b>
		•		7,3	∪ <del>+</del>		•	7	40			_		50					760				
C	GAT CTA	TT	GG	TG '	TTC	TT	'A A	CA	C N T		~~	• ১C:		TT TT			<b>*</b> .		•		•		
C														УУ Т.Т.	ACA	G	TA ber	CAI	A C	AA	TAC	AA	/C
	D	L	1	V	F	L		T	D	(	3	T	- 4	I	T		v. V	ں 175	r. C.	TT	ATG Y	TI	rG
															_		-	~	,	2	Y	<b>1</b> /	<b>≀&gt;</b>

FIGURE 34 (2 of 4)

78//33

#### B-31 OSP B / B-31 P41 (122-295)

										٠.					
770			780			7	90			800	•		810	)	
•		●.	•		•		•	•		•		•	•		•
ACA	GCT	GGA	ACC	AGC	CTA	GÁA	GGA	TCA	GCA	AGT	GAA	ATT	ALL	AAT	
TGT	CGA	CCT	TGG	TCG	GAT	CTT	CCT	AGT	CGT	TCA	CTT	TAA	Tri	ጉጥል	GÀÀ
		G	T	s	L	E	G	s	A	S	E	ī		N	L>
	-		-	_	_	_	_	- T.	••	_	-	•	**		حــ
8:	20			830			840			8	50		•	860	
	•	•		*			•		•	•		•		•	
TCA	GAG	CTT	AAA	AAC	GCT	TTA	AAA	GGT	CAC	CCC	ATG	CCT	C 3 3	ጥእጥ	AAC
AGT	CTC	GAA	TTT	TTG	CGA	AAT	TTT	CCA	GTG	GGG	TAC	CCA	_ CWV	1771	TTG
s	E	L	ĸ	N	A	L	K	G	H	P	M	7	911	Y	116
_	_	_		•	••	_		•		. •	====	•	Q	Ι.	1//>
	870			81	80		1	890		*	900				10
•	•		•		•	•		*		•	-		•		. U
CAA	ATG	CAC	ATG	TTA	TCA	AAC	AAA	TCT	CCT	тст	CAA	አኔጥ	GTL	AGA	200
GTT	TAC	GTG	TAC	AAT	AGT	TTG	TTT	AGA	CGA	202	CTT	TTE	CAT	TCT	2000
		н	M	L	s	N	ĸ	S	Δ	5	.0	N	V	R	
<u> </u>		•••	,	. ,	_	. ••	••	•	•		. •	14	٧	K	T>
		920			930			94	10		(	950			960
• . •				*	•		•		•	•		•		•	-
GCT	GAA	GAG	CTT	GGA	ATG	CAG	CCT	GCA	AAA	ATT	AAC	ACA	CCA	GCA	TC2
CGA-	CTT	CTC	GAA	CCT	TAC	GTC	GGA	CGT	TTT	TAA	TTG	TGT	GGT	CGT	36~
A	E	E	L	G	M	Q	P	A	K	I	N	T	P	A	5>
	•											_	_	•••	
		9	70		9	980			990			100	00		
	٠.		•	•		•		•	•		•		•	•	
CTT	TCA	GGG	CTT	CAA	GCG	TCT	TGG	ACT	TTA	AGA	GTT	CAT	GTT	GGA	GCA
GAA	AGT	CCC	GAA	GTT	CGC	AGA	ACC	TGA	AAT	TCT	CAA	GTA	CAA	CCT	CGT
L	S	G	L	Q	A	S	W	T	L	R	v	H	v	G	2>
1010			1020			103	30		10	040		1	1050		
		• .	•		•		*	*	•	•		•	•		•
ACC	CAA	GAT	GAA	GCT	ATT	GCT	GTA	AAT	ATT	TAT	GCA	GCT	AAT	GTT	GCA
		CTA	CTT	CGA	TAA	CGA	CAT	TTA	TAA	ATA	CGT	CGA	TTA	CAA	CGT
T	Q	Ŋ	E	A	I,	A	v	N	I	Y	A	A	N	v	A>
106	. ^			20			000								
100	*		Τ.	70			1080		_	109	70		13	100	
<b>ה</b> ממ	بلمان	Δυ. 	m∕		C > C	- -		~	`~		•			•	
ጥጥል	CYY	770	101	CCX	CTC	CCT	CCI	CAA	ACT	GCT	CAG	GCT	GCA	CCG	GTT
N	t.	r.	707	CCA	CIC	CC1	CGA	GII	TGA	CGA	GTC	CGA	CGT	GGC	CAA
•	~	•	•	G	<b>E</b>	G	Α.	Q	.1	A	Q	A	A	P	V>
3	110			112	20		11	130		•	140				
•	•		•		*	•		*		•	-740		•	115	
CAA	GAG	GGT	GTT	CAA	CAG	GAA	GG A					CC 2		GCT	
GTT	CTC	CCA	CAA	GTT	GTC	CTT	CCT	CCF	Cur	CTC	CCM	COT	CCT	CGA	WCW
0	E	G	v	0	0	£.	G	)	211	310	201	201	20H	A	1.01

FIGURE: 34 (3 of 4)

#### B-31 OSP B / B-31 P41 (122-295)

	1160				1170			1180			1190				1200		
•		•		•	•	•	•		• .	•	•	•		•	•		
GCA	CCT	TCT	CA	A GGC	: GG/	GTI	CAA "	TC	r cc:	r GT	CAA 1	GT	בא ז	AC	T ACA		
CGT	GGA	AGA	GT	r ccc	CCT	CAP	TT?	AG2	A GG	A CA	A TTA	CA	1 76	TG	A TGT		
Α	P	S	Q	G	G	v	N	S	P	V	N	V	T	T	<b>T</b> >		
•	1210				1220				1230	)	1240						
	*		•	. •	• •		•		•		•				•		
GTT	GAT	GCT	AA!	r ACA	TC	CTI	GCI	' AAJ	ATT	r GA2	TAA A	, eci	AT:	` AG	ATG		
CAA	CTA	CGA	TŢ	A TGI	, YC1	GAA	CGA	TT	LAT 1	CIT	TTA	CGA	TA	TC	TAC		
v	D	A	N	T	s	L	A	K	I.	E"	N.	A	I	R	M>		
1250 1260					1270				1280			1000					
•	•		-				* •			123							
አጥክ ን	CT .												•		•		
ATA A	CA (	CTA	CAA	TCC	CCT	AAT	TTA	GGT	GCT	TTC	CAA	AAT	AGA	CTT	GAA		
TAT T	c .	רוא	011	100	7	114	WWI	CCA	CGA	AAG	GTT	TTA	TCT	$G\lambda\lambda$	CTT		
•	3		v	Α.	^	14	υ.	G	A	F	Q	N	R	ī	E>		
1300 1310				310		. 1	320	13			30 1						
•	•						_		-		•	•		•			
TCT A	TA :	AAG	AAT	AGT	ACT	GAG	TAT	GCA	ATT	GAA	AAT	CTA	AAA	GCA	エーエ		
AGA T	'AT :	rrc	TTA	TÇA	TGA	CTC	ATA	CGT	TAA	CTT	TTA	CAT	خخمك				
s	I	K	N	S	T.	Ε	Y	A	I	E	N	L	K	À	S>		
1350 136														٠.			
				150			•										
TAT G	CT (	CAA	ATA			c											
ATA C																	
						. –											

FIGURE 34 (4 of 4)

B-31 OSP B/ B-31 P41 (140-234) Sequence Range: 1 to 1141

		•		10		•	20		•	3	0	•		40		
	GC	A CA	AA A	A GGT	r GC:	C GAC	TCA	ATT	r GG:	· T TC	T CA	A A 2 :	A C A		T ()	T CTA
	CO 1	. 611		1 664	4 66/	1 616	- AGI	TA	א ככז	A AC	יידים ב	ملحك ملا	T (7)		1 0m	
	λ	Q	K	G	A	E	s	I	G	s	Q	ĸ	E	N	D	A GAT
•	50			60			٠.	70		•	80			9	0	
								•			•		•		•	•
	TTG	CAL		י כידני	. 101	AG1	*	AAA	TCA	CAT	CAZ	AA.	GC	גג ז	A CA	A GAC
	N	L	E	D	, non	. 164		111	. AG1	GTZ	GTT	TTC	CG	1 TT	r GT	A GAC CTG D>
	•	_	_	-				K		H	Q	N	A	K	Q	D>
	1	00		110								.30		140		
		•	•		. *		•	•		•		•		,	_	
	CTT	CCT	GCG	GTG	ACA	GAA	GAC	TCA	GTG	TCI	TTC	TTT	` AAT	GG:	CAA 1	<b>656</b> 7
	~, ~,	- UUA					1110	ACTO		7. ~ 3						
		F	^ .	. •	1	£	D	5	V	s	L	F	N	G	N	X TTT K>
		150			1	60	•		170			180			,	0.0
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	GCA	ACA	ATT	GAT	CAG	GTT	GAA	CTT	AAA	GGA	ACT	TCC	GAT	AAA	AAC	AAT
	-0.	101	*~~	CIM	GIL	CAA	Ciri	GAA	TTT	CCT	TGA	ACC	CTA	سلسك		-
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	CCF	707	CCT	TOO	CNA	GAA	GGT	TCA	AAG	CCT	GAC	AAG	AGT	AAA	GTA	AAA
	G	s	G	T	L	CII	CCA	AGT	TTC	GGA	CTG	TIC	TCA	TII		AAA TTT
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	and y		•			*	2	•	•		*		•	_		•
	AAT	TCT	CYV	TCT	GCT	GAT	TTA	AAC	ACA	GTA	ACC	TTA	GAA	GCA	TTT	GAT
				ハウハ	COA	CIM	AAT	1-14:	TYZT	ידימי		2 2 00				
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340		350			360					37						
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	CCC	TCC	AAC	CAA	AAA	ATT	TCA	AGT	AAA	GTT	ACT	AAA	AAA	CAG	GGG	TCA
	••	J		Q		Ŧ	,5	S	K	V	T	K	K	Q	G	AGT S>

#### B-31 OSP B/ B-31 P41 (140-234)

	390			4	00		•	410		•	420			4	30
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	T														
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. ACA	AGA	TCA	AAC	GGA	ACT	ACA	CTT	GAA					ACA	CAT	CCT.
TGI	TCT	AGT	TTG	CCT	TGA	TGT	GAA	CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
T	R	s	N	G.	T	T	Ĺ	E	Y	S_	_Q.	I	T	D	A>
•		49	90	•		500			510			5:	20		
	•		•	•		•		•	•		•		•	•	
	TAA														
CTO	TTA	CGA	TGT	TTT	CGT	CAT	CII	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
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530		_	540	_		. 55	50			560			570		
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CTI	CCT	TCA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TTT	CTT	CCA
E	G	s	L	v	v	G	K	T	T	v	E	I	K.	E	G>
· ·	80			590			500		•	61	١.				
<u>*</u> 5	80	•	:	590			600		•	61	LO	•	. (	520	
ACT	GTT	ACT	CTA	AAA	AGA	• GAA	ATT	GAA	AAA	GAT	GGA	* AAA	GTA	AAA	GTC
ACI TGA	GTT CAA	TGA	CTA GAT	AAA TTT	TCT	GAA CTT	TTA	GAA CTT	AAA TTT	GAT CTA	GGA CCT	AAA TTT	GTA CAT	AAA TTT	CAG
ACI TGA	GTT	TGA	CTA GAT	AAA TTT	TCT	GAA CTT	ATT TAA I	GAA CTT E	AAA TTT K	GAT CTA	GGA CCT	AAA TTT	GTA CAT	AAA TTT	CAG
ACI TGA	GTT CAA	TGA T	CTA GAT	AAA TTT K	TCT	GAA CTT	ATT TAA I	GAA CTT E	AAA TTT K	GAT CTA D	GGA CCT G	AAA TTT K	GTA CAT V	AAA TTT	CAG V>
ACT TGA T	GTT CAA V	TGA T	CTA GAT L	AAA TTT K	TCT R	GAA CTT E	ATT TAA I	GAA CTT E	AAA TTT K	GAT CTA D	GGA CCT G	AAA TTT K	GTA CAT V	AAA TTT K	CAG V>
ACI TGA T	GTT CAA V 630	TGA T	CTA GAT L GAC	AAA TTT K 64	TCT R 10 • GCA	GAA CTT E	ATT TAA I	GAA CTT E 50	AAA TTT K	GAT CTA D	GGA CCT G 660	AAA TTT K	GTA CAT V	AAA TTT K 67	CAG V>
ACI TGA T	GTT CAA V 630 TTG AAC	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 10 • GCA	GAA CTT E GGT CCA	ATT TAA I TCT AGA	GAA CTT E 550 AAC TTG	AAA TTT K AAA TTT	GAT CTA D	GGA CCT G 660 ACA TGT	AAA TTT K GGT CCA	GTA CAT V AAA TTT	AAA TTT K 67 TGG ACC	CAG V> 70 GAA CTT
ACI TGA T	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 10 GCA CGT A	GAA CTT E GGT CCA G	ATT TAA I TCT AGA	GAA CTT E 50 AAC TTG N	AAA TTT K AAA TTT K	GAT CTA D	GGA CCT G 660 ACA TGT	AAA TTT K GGT CCA	GTA CAT V AAA TTT	AAA TTT K 67 TGG ACC W	CAG V> 70 GAA CTT E>
ACI TGA T	GTT CAA V 630 TTG AAC L	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 10 • GCA CGT	GAA CTT E GGT CCA G	ATT TAA I TCT AGA	GAA CTT E 550 AAC TTG	AAA TTT K AAA TTT K	GAT CTA D	GGA CCT G 660 ACA TGT	AAA TTT K GGT CCA	GTA CAT V AAA TTT	AAA TTT K 67 TGG ACC W	CAG V> 70 GAA CTT
ACT TGA T TTT AAA F	GTT CAA V 630 AAC L AGT	TGA T AAT TTA N 680 ACT	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T	TCT R 10 GCA CGT A 690 TTA	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S	GAA CTT E 550 AAC TTG N 70	AAA TTT K AAA TTT K	GAT CTA D * AAA TTT K	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G	GTA CAT V AAA TTT K	AAA TTT K 67 TGG ACC W _	CAG V> 70 GAA CTT E> 720
ACT TGA T TTT AAA F	GTT CAA V 630 AAC L AGT TCA	TGA T AAT TTA N 580 ACT TGA	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 10 GCA CGT A 690 TTA AAT	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S ATT TAA	GAA CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K AAA TTT K OO GCT CGA	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G AAA TTT	GTA CAT V AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> O GAA CIT E> 720 AAA TIT
ACT TGA T TTT AAA F	GTT CAA V 630 AAC L AGT	TGA T AAT TTA N 580 ACT TGA	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 10 GCA CGT A 690 TTA AAT	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S ATT TAA	GAA CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K AAA TTT K OO GCT CGA	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G AAA TTT	GTA CAT V AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> O GAA CIT E> 720 AAA TIT
ACT TGA T TTT AAA F	GTT CAA V 630 AAC L AGT TCA	TGA T AAT TTA N 880 ACT TGA T	CTA GAT L GAC CTG D AGC TCG S	AAA TTT K 64 ACT TGA T ACT TGA T	TCT R IO GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G ACA TGT T	ATT TAA I TCT AGA S ATT TAA	GAA CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K AAA TTT K GCT CGA A	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G AAA TTT	GTA CAT V AAA TTT K AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> O GAA CIT E> 720 AAA TIT
ACT TGA T TTT AAA F GAC	GTT CAA V 630 AAC L AGT TCA S	TGA T AAT TTA N 680 ACT TGA T	CTA GAT L GAC CTG D AGC TCG S	AAA TTT K 64 ACT TGA T ACT TGA T	TCT R IO GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G ACA TGT T	ATT TAA I TOT AGA S ATT TAA I	GAA CTT E 50 AAC TTG N 70 AGT TCA S	AAA TTT K AAA TTT K GCT CGA A	GAT D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G 10 AAA TTT K	GTA CAT V AAA TTT K AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> 70 GAA CTT E> 720 AAA TTT K>
ACT TGA T TTT AAA F GAC CTC D	GTT CAA V 630 AAC L AGT TCA S	TGA T AAT TTA N 680 ACT TGA T GTG	CTA GAT L GAC CTG D AGC TCG S	AAA TTT K 64 ACT TGA T ACT TGA T	TCT R 10 GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G ACA TGT T	ATT TAA I TCT AGA S ATT TAA I	GAA CTT E 50 AAC TTG N AGT TCA S	AAA TTT K AAA TTT K GCT CGA A 750	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T AGC TCG S	AAA TTT K GGT CCA G 10 AAA TTT K 76	GTA CAT V AAA TTT K AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA T	CAG V> O GAA CTT E> 720 AAA TTT K>
ACT TGA T TTT AAA F GAC CTG	GTT CAA V 630 AAC L AGT TCA S	TGA T AAT TTA N 680 ACT TGA T GTG CAC	GAC CTG D AGC TCG S 30 TTC AAG	AAA TTT K 64 ACT TGA T ACT TGA T	TCT R 10 GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G ACA TGT T	ATT TAA I TCT AGA S ATT TAA I GGT CCA	GAA CTT E 50 AAC TTG N AGT TCA S	AAA TTT K AAA TTT K GCT CGA A 750 ATT	GAT CTA D * AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T AGC TCG S	AAA TTT K  GGT CCA G 10 AAA TTT K  76 CAA GTT	GTA CAT V AAA TTT K AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA T TAC ATG	CAG V> 70 GAA CTT E> 720 AAA TTT K>

FIGURE 35 (2 of 3)

#### B-31 OSP B/ B-31 P41 (140-234)

	770			780										810	)	,
	<b>NCN</b>	CC#	•			•							• .	•	•	•
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			ىلىك <u>«</u>			CCT		*		*		• 5	•		•	
	AGT	CTC	GAA	TTT	TTG	CCY	TIM	ተተጥ ተ	CCA	CAC		ATG	GCI	TCI	CAA	AAT TTA
	s	E	L	ĸ	N	Α.	L	ĸ	G	H	P	M	. CGA	. AGA	GTT	TTA <n< td=""></n<>
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	CTA	202	እሮአ	~ *	C	•	•	663	*		•	•		*		
	CAT	TCT	TGT	CCA	CTT	CTC	CII	CCT	ATG	CAG	CCT	GCA	AAA	ATT	AAC	ACA TGT
	V	R	T	A	Ē	E	L	G.	M	010	GGA P	. CG1	TTT.	TAA	TTG N	TGT
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	_	:	920			930			· 9.	40			950		•	960
	CCA	GC A	שר.»	C.D.D.	TC N	•		•		•	*		•			
	GGT	CGT	AGT	GAA	AGT	CCC	CII	CAA	CGC	TCT	TGG	ACT	ATT	AGA	GTT CAA	CAT
	P	Α	s	L	s	G	L	0	A.	S	W	TGA	AAT	TCT	V	GTA
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			97	70	_	•	980			990	-		100	00		
	GTT	GGA	GC A									*			•	
	CAA	CCT	CGT	TGG	GTT	CTA	CTT	CGA	ALL	CGA	CAT	AAT	ATT	TAT.	GCA CGT	GCT
	v	G	Α	T	Q	D	E	A	I	A	V	N	T	ATA	A	CGA
															•	27
10	10		. 1	.020		•	103	0		10	10		3	.050		
	AAT	GTT	GCA	TAA	СТТ	<u>ተ</u> ተር	ىلىك	GGT.	CAC	CCX	*		•	• .	CAG	•
	114	CAA	COL	TTA	GAA	AAG	AGA	CCA	CTC	CCT	CCA	CTT	TO A	~~ 1	~~~	~~`
	N	v	Α	N	L	F	s	G	Ε	G	A	0	T	A	Q	CGA CA
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	106	*	•	10	*			080			109	90			.00	
	GCA	CCG				GGT	GTT	CAA	CAG		CCA	*	C	~ ~	•	GCA
	CGI	حور	CAA	G.L.T.	CTC	CCA	CAA	GIT	GTC	CTT	CCT	CGA	CTT	CTC	CCT	CCT
	Α	P	V.	Q	E	G	v	Q	Q	E.	G	A	Q	0	P	A>
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					CCT					ىئىن			_			
	GGA	CGA	TGT	CGT	GGA	AGA	GTT	CCG	CCT	CAA	CCA	GTG	G			
	P	A	T	A	P	s	Q	G	G	v	G	н	X>	÷		

FIGURE 35 (3 of 3)

B-31 OSP B/ B-31 P41 (140 -295)

Sequence Range: 1 to 1324

10 20 30 · GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT A Q K G A E S I G S Q K E N D L> 50 60 70 80 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 110 100 120 130 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT. AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 150 160 170 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 220 230 200 210 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A TIDQVELKGTSDKN N> 250 260 270 280 . • GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT T L E G S K P D K S K V K> G 290 300 310 320 330 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 350 360 370 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT ASNQKISSKVTKKQGS>

FIGURE 36 (1 of 4)

### B-31 OSP B/ B-31 P41 (140 -295)

•	390	•	•		00-	•		410		•		•			430
ATA	ACA	A GAC	GA	ACT	CTC	AAA:	GCI	` AA7	AA 1	A TT	A GA	C TC	A AA	G AA	A TTI
141	161	CIC	- 017	10,	GAG	TTT	, CCY	TT	TT	r aa:	CTO	GAG	TT		ጥ አክባ
. I	T	E	E	T	L	K	A	. <b>N</b>	K	L	D	s	K	K	L
		440			450			4				470			480
. •		•		•	•		•		•	·	•			•	
ACA	AGA	TCA	AAC	GGA	ACT	, ycy	CTT	GAA	TAC	TCA	CAJ	ATA	A ACA	A GAT	
101	101	WG T		, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	TUA	TGT	GAA	(-1-1-	' אידר	ב אכיד	, 6		T		
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		4	90			500			510			5	520		
	•		•	•		•		•	*		•		•	•	,
GAC	AAT	GCT	' ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	AAT	` AGC	ATT	' AAG	CTT
C 1 0	* * *	COM		111		CAT	CTT	TGA	೧೬೬	ىلىنىلى ر	الاستبالية	TOO	- m	-	
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GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	' AAA	GAA	
~ · ·	~~~	1	$\sigma \alpha \alpha$	CVI	LAG	CUT	1-1-1	TCT	ستاست	-csc		m 2 2	~~~		
E	G	۵	L	V	V	G	K	T	T	v	E	I	K	E	CCA G>
	30		:	590	•		600		•	6	10			620	
	•	•		•		•	•		•		•	•		_	
ACT	GTT	ACT	CTA	AAA	AGA.	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	AAA	GTC
107		IGA	CAI	1.1.1	TCT	CTT	TAA	CTT	TTT	$CT\Delta$	$CC_{-}$	مذملت	~ > ~		
•	•	1	1.	V	K	E	. I	E	K	D	G	K	v	K	V>
	630			. 64	0		6	50			660				
•	•		•		•	•		•		•			•		70
TTT	TTG	AAT	GAC	ACT	GCA	GGT	TCT	AAC	AAA	AAA	ACA	GGT	AAA	TGG	GAA.
	~~	IIA	C16	IGA	CG.I.	CCA	AGA	TTG	TTT	TTT	$\Delta C \Delta C$	CCA	كالمكمكة	100	~~~
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GAC .	AGT	ACT	AGC	ACT	TTA	ACA	שייים ב	ACT	CCT	GAC	AGC	AAA	444	у С-Т.	277
		100	7 60	104	~~1	1101	TAA	TCA	CCY		TOO	T C C C C C C C C C C C C C C C C C C C			
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GAT '	TTG	GTG	TTC	TTA	ACA	GAT :	сст	202	ን ፈኮሌ	ACA	CTA	CDN		# m h C :	
~	-A-C	CAC	AAG	WWI	161	CTA	CCA	TGT	TAA	<b>エCエ</b>	CAT	GTT	CAA	ATC	AAC
D	L	v	F	L	T	D	G	T	I	T	v	Q	0	YIG.	
													-	-	

FIGURE 36 (2 of 4)

### B-31 OSP B/ B-31 P41 (140 -295)

	770				780	)			790			80	<b>1</b> 0					-
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	8	320				830			84				85	50			860	
	T/C 1		~ ~	- T		•		•	•		•			•		•	•	,
	7 (7	CT.	6 C	7.T.	AAA	AAC	GC	TTA	LAA	A GG	T CA	CC	CC	ATC	ec.	TC	T CA	A AAT
	S	E	<b>.</b> .	aa L	K	N	N CGA	L	. 111. V	r cc.	A GI	G G	GG ==	TAC	CG	A AG	à GI	A AAT
	~	_		_	K	M	^	L	K	G	н		P	M	Α	S	Q	N>
		87	0			8	80			890				900	)			910
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	CCA	GCA	T	CA	CTT	TCA	GGG	CTT	CAA	GCG	TC	r To	G ,	ACT	TTA	AGA	GT	_
		CGT A	- ^	3 1	CAA	MOI	ccc	GAA	GTT	CGC	AGA	A AC	:C '	TGA	AAT	. J.C.	CA	r cat A gta
	P	A	•	5	L	S	G	L	Q	A	S	8	?	T	L			H>
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	GTT	GGA	GC	A.	ACC	CAA	GAT	GAA	GCT	ATT	GCI	`GT	A	TAF	ATT	TAT	פרי	GCT
	···		Ų	, 1	100	011	CIM		CGA	TAA	CGA	$\sim$ $\sim$ $\sim$	ጥ ባ	AT	TAA	ATA	CGI	GCT CGA
	٧	G	A		T	Q	D	E	Α	I	A	v		N		Y		A>
1 (	010			1	020			103	30		. 1	0.4.0		•				
	•		•		•		•		•						_	1050		_
	AAT	GTT	GC	A i	TAA	CŤT	TTC	TCT	GGT	GAG	GGA	GC	r c	'AA		CCT	CAC	GCT
			-0	•	117	CAA	MAG	AGA	CCA	CIC	CCT	CG	A C	T-T-	TCA	CCA	CTC	~~ .
	N	- <b>V</b>	Ą		·N	-L	F	S	G	E	G	A		Q	T	A	Q	۸>
	106	0			10				080									
		•		•		•		•			*		90		_		100	
	GCA	CCG	GT	T	AA	GAG	GGT	GTT	CAA	CAG	GAA	GG		~	۳ د د ت			
٠																		
	A	₽	V		Q	E	G	v	Q	. Q	E	G		A	0	0	P	A -
		110														•	•	
						112	•	♣.	11	.30				40				50
	CCT	GCT	AC.	A G	CA (	CCT	TCT	CAA	ccc	CCN	~m~	*		*		•		
						SGA.	AUA	C-1"1"	1772	7	$\sim$ $\sim$ $\sim$	(T)	• •	~ .			AAT	GTT
	P ·	A	T		Α	P	5	Q	G	G	V	T TA	· A	GA ( C	Aکی	CAA		
								-	_	_	*	14.	•	J	٢	V	N	V>

FIGURE 36 (3 of 4)

### B-31 OSP B/ B-31 P41 (140 -295)

	1	160			1170			11	80		1	190			1200
•		•	•	•	•		•;		•	ŧ		•		•	
ACA TGT	ACT TGA	ACA TGT	GTT CAA	GAT CTA	GCT CGA	AAT TTA	ACA TGT	TCA AGT	CTT	GCT	AAA	ATT	GAA	AAT	GCT
T	T,	T	v	D	A	N	T	s	L	A	К	_	E		A>
		12:	10		1:	220			1230	•		124	d D		
	•		•	•		•		•	•		•		•	•	
ATT	AGA	ATG	ATA	AGT	GAT	ĊAA	AGG	GCA	AAT	TTA	GGT	GCT	TTC	CAA	AAT
TAA	TCT	TAC	TAT	TCA	CTA	GTT	TCC	CGT	TTA	AAT	CCA	CGA	AAG	GTT	TIA
I	R	M	I	s	D	Q	R	A	N	L	G	A	F		N>
1250		2	1260			127	70	-	12	280		,	1260		
		•	•		•	127	•	•	12	•		•	1290		
AGA	CTT	• GAA	TCT	ATA	+ AAG	AAT	* AGT	ACT	GAG	TAT	GCA	ን ተብ •	•	AAT	CTA
AGA TCT	GAA	GAA CTT	TCT AGA	ATA TAT	AAG TTC	AAT ATT	AGT TCA	TGA	GAG CTC	TAT	GCA CGT	ን ተብ •	•	AAT TTA	CTA GAT
AGA TCT	CTT GAA L	GAA CTT	TCT AGA	ATA TAT I	AAG TTC	AAT ATT	AGT TCA	TGA	GAG CTC	TAT	GCA CGT A	ን ተብ •	GAA CTT	TTA	CTA GAT L>
AGA TCT	L	GAA CTT	TCT AGA	TAT	AAG TTC	AAT TTA N	AGT TCA S	TGA	GAG CTC	TAT ATA	CGT	• TTA	GAA CTT	TTA	GAT
AGA TCT R	L	GAA CTT	TCT AGA S	TAT	AAG TTC	AAT TTA N	AGT TCA	TGA	GAG CTC	TAT ATA	CGT	• TTA	GAA CTT	TTA	GAT
AGA TCT R 130	L DD GCA	GAA CTT E	TCT AGA S	TAT I 310 GCT	AAG TTC K	AAT TTA N	AGT TCA S	TGA T	GAG CTC E	TAT ATA	CGT	• TTA	GAA CTT	TTA	GAT
AGA TCT R 130	L DD GCA	GAA CTT E	TCT AGA S	TAT I	AAG TTC K	AAT TTA N	AGT TCA S	TGA T	GAG CTC E	TAT ATA	CGT	• TTA	GAA CTT	TTA	GAT

FIGURE 36 (4 of 4)

Osp b/ fla (122-234) osp c Sequence Range: 1 to 1765

		. ]	LO			20		٠	30				40		
	•		•	•		•		•	. •		•		• •	•	
			GGT												
			CCA												
A	Q	K	G	Α	E	S	1	G	S	Q	K	E .	X	Ď	L>
			60				70			80			90		
. 20		•	•				•	•		_•		•	•		•
	CTT	GAA	GAC.	TCT	AGT	AAA	ÄAA	TCA	CAT		AAC	GCT	222	CAA	GAC
			CTG						••		•-				
	L		D												
•				•					•		•				
10	00		3	110			120			13				140	
	•	•		•		• '	•		•		•	•		•	
			GTG												
			CAC V												
L	P	A	V	1	E	D	5	V	3	L	r	. N	Ŀ	V	K>
	150			16	50		1	170			180			19	<b>:</b> 0
• ,	*		•			•		•		*	•		•		•
ATT	TTT	GTA	AGC	AAA	GAA	AAA	TAA	AGC	TCC	GGC	AAA	TAT	GAT	TTA	AGA
TAA		-	TCG										CTA	AAT	TĊT
I,	F	V	S	ĸ	E	K	N	S	S	G	K	Y	<b>&gt;</b>	L	₹>
		200			210			22	מי		_	30			240
	•	200		•	210		•	24		•	-	230			240
GCA	ACA	ATT	GAT	CAG	GTT	GAA	CTT	AAA	GGA	ACT	TCC	GAT	AAA	AAC	AAT
-	-		CTA	,											
A	T	I	D	Q	v	E	L	K	G	T.	s	D	X.	N	N>
		2	50		- 7	260		_	270		_	28	35		
	mcm.	CC }	ACC	C.II.II.	CNA	CCT	TO N	220		C \ C		<b>.</b>	•	~~`	
	-		TGG												
			T									s		v	K>
-	_	_	_						_	_		_	•		
290			300			3:	10		3	320			330		
•		•	•		•		•	*	•	•		•	•		•
												·			GAT .
			AGA												
مد	1	V	s	^	ט	L	14		V	1	L	£	٨	F	אכע
3	40			350			360			3 7	70		-	380	
	40														
	40	•					•		•		•	•		•	
	•	•		•		•					• AAA	AAA		•	TCA
GCC	AGC TCG	AAC TTG	CAA GTT	AAA TTT	ATT TAA	TCA AGT	AGT TCA	ÄAA TTT	GTT CAA	ACT TGA	TTT	TTT	CAG GTC	GGG CCC	

FIGURE 37 (1 of 5)

Osp b/ fla (122-234) osp c

	390			. 4	00			410			420	1			
•	•		•		•	•	,	•					•		130
ATA	ACA	GAG	GAA	ACT	CTC	AAA	GCI	LAA	. AA	ATŢ.	GAC	TC	AAC	AA	TTA
TAT	161	CIC	CTT	TGA	GAG	TTI	, CGY	. TTA	LIL	AAI	, CIG	AGT	TTC	. TT-	ጉ አአጥ
I	T	E	E	T	L	K	A	N	K	L	D	S	K	ĸ	L>
		440			450		•								
•		440		•	450				6D			470			480
ACA	AGA	TCA	AAC	GGA	ACT	ACA	ىلملى					*		•	• GCT
TGT	TCT	AGT	TTG	CCT	TGA	TGT	GAA	CTT	ATG	AGT	CAA	ጥልጥ የነላ	ACA TOT	GAT	GCT CGA
T	R	S	N	G	T	T	L	E	Y	s	0	I	T		A>
						•				<u> </u>		-	•		N,
		<b>. 4</b> .	90		!	500			510			5	20		
636			•	•				*	•		•		•	•	
CTG	ሊሊገ ጥጥል	CCA	ACA TOT	AAA	GCA	GTA	GAA	ACT	CTA	AAA	TAA	AGC	ATT	AAG	CTT
D	N	A	7G2	111	7	CAT	CTT	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
	••	••	. * ′		Α.	•	£	7		K	N	S	1	K	L>
530			540			5	50			560			570		
•		•	•		•		•	*		•		•			•
GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	AAA	GAA	GGT
CII	CCT	TCA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TIT	CTT	CCA
£	G	S	L	V		G	K	T	T	v	E	I	K	Ē	G>
. 58	30	•	5	590			600			6:			,		,
	•	•	_	•		•	•		•	0.	•		•	520	
ACT	GTT	ACT	CTA	AAA	AGA	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	222	GTC
IGA	CAA	TGA	GAT	TTT	TCT	CII	TAA	CTT	TTT	CTA	CCT	TTT	CAT	TTT	CAG
T	V	T	L	K	R	E	I	E	ĸ	D	G	K		K	
	630			6.4			,								
•	•		• 1	0 7	*	•		50		•	660		_	67	70
TTT	TTG	TAA	GAC	ACT	GCA	GGT	TCT	AAC	AAA	AAA	101	GGT.	222	TCC	
AAA	AAC	TTA	CTG	TGA	CGT	CCA	AGA	TTG	TTT	TTT	TGT	CCA	لتتل بحت	ACC	CAA
F	L	N	D	T	A	G	s	N	K	K	T	G	K	W	E>
	_	80			<b>COO</b>				_						
*	-	. *		•	690			70	0	_	7	10			720
GAC	AGT	ACT	AGC	ACT		ACA	₹ dods	እርጥ	- -	C1C		•		•	•
CTG	TCA	TGA	TCG	TGA	AAT	TGT	TAA	TCA	CGA	CTC	AGC TOO	AAA	AAA	ACT	AAA TTT
D	s	T	S	T	L	T	I	s	À	D	S	K	111	TGA	TTT
											-	••	••	•	~~
	_	73	0	_		40			750			76	0		
CAT	تىلىت م	GTC		Unun y		*			*		•		•	•	
CTA	AAC	GTG	TIC	TIA	TOT	GAT CTA	CCN	ACA	ATT	ACA	GTA	CAA	ርኢአ	TAC	AAC
D	L	CAC V	F	L	T	CIN	G	TGT	TAA	TGT .	CAT	GTT	Ġī.	ATG	
			-	_	-	_	9	-	-	≖ .	V	Q	Q	Y	N>

Osp b/ fla (122-234) osp c

7	70			780			79	90		1	300	-		810		
	•		•	•		•		•	•		. •		.•	•		•
															AAT	
	TGT	CGA	CCT	TGG	TCG	GAT	CTT	CCT	AGT	CGT	TCA	CTT	TAA	TTT	TTA	GAA
	T	A	G	T	S	L	E	G	S	A	S	E	I	Y.	N	L>
	82	20		8	330			840			85	50		1	B60	
		•	<b>₽</b> €		•		•	•		•		•	•		•	
															AAT	
															TTA	
	S	E	L	K	N	. A	_ L·	K	G	- <b>.H</b> .	_P_	М	G	К	N	S>
•		870	•		88	30		1	390			900	•		93	0
	•	*		•		*	•		7		•	•		•		•
															GTT	
															CAA	
	G	K	D .	G	N	T	S	Α	N	S	A	D	E	Ξ	v	K>
			920			930			94	10	. 7	٠.	50			960
	•		٠,	•	•	•		•	• •	*	*		•		•	*
															AAT	
															TTA	
, racer	G	P	N	L	T	E	I	S	- <b>K</b>	K	I	T	Ð	٤	N	A>
. **			0.				900			000			100			
. • •		•	9	70	•	9	980			990	•	•	100	00		
.**	GTT	TTA		•	GTG		•		•	•,		• CTG		•.	ATA	GAT
. **			CTT	GCT		AAA	GAG	GTT	• GAA	GCG	TTG		TCA	TCT	ATA	
	CAA	AAT	CTT GAA	GCT CGA	CAC	AAA TTT	GAG CTC	GTT CAA	• GAA CTT	GCG CGC	TTG AAC	GAC	TCA AGT	TCT AGA	ATA TAT I	CTA
• •	CAA V	AAT	CTT GAA L	GCT CGA A	CAC	AAA TTT K	GAG CTC E	GTT .CAA V	GAA CTT E	GCG CGC A	TTG AAC L	GAC	TCA AGT S	TCT AGA S	TAT	CTA
10	CAA	AAT	CTT GAA L	GCT CGA	CAC	AAA TTT K	GAG CTC E	GTT CAA V	GAA CTT E	GCG CGC A	TTG AAC L	GAC L	TCA AGT S	TCT AGA S	TAT	CTA
10	CAA V )10	AAT L	CTT GAA L	GCT CGA A	CAC V	AAA TTT K	GAG CTC E	GTT CAA V	GAA CTT E	GCG CGC A	TTG AAC L	GAC L	TCA AGT S	TCT AGA S	TAT	CTA D>
10	CAA V 010 GAA	AAT L ATT	CTT GAA L GCT	GCT CGA A 1020 GCT	CAC V	AAA TTT K	GAG CTC E 10:	GTT CAA V	GAA CTT E	GCG CGC A	TTG AAC L )40	GAC L CAC	TCA AGT S	TCT AGA S LOSO	TAT I TAT	CTA D>
10	CAA V 10 GAA CTT	AAT L ATT TAA	CTT GAA L GCT CGA	GCT CGA A 1020 GCT CGA	CAC V AAA TTT	AAA TTT K GCT CGA	GAG CTC E 101	GTT CAA V 30 GGT CCA	GAA CTT E	GCG CGC A 1(	TTG AAC L 040 ATA TAT	GAC L CAC GTG	TCA AGT S CAA GTT	TCT AGA S 1050 AAT TTA	TAT	CTA D>  GGT CCA
10	CAA V 010 GAA CTT E	AAT L ATT TAA I	CTT GAA L GCT CGA A	GCT CGA A 1020 GCT CGA A	CAC V AAA TTT K	AAA TTT K GCT CGA	GAG CTC E 103 ATT TAA I	GTT CAA V 30 GGT CCA G	GAA CTT E AAA TTT K	GCG CGC A 1(	TTG AAC L 040 ATA TAT I	GAC L CAC GTG H	TCA AGT S CAA GTT	TCT AGA S 1050 AAT TTA N	TAT I TAA TAA ATT	CTA D> GGT CCA
10	CAA V 010 GAA CTT E	AAT L ATT TAA	CTT GAA L GCT CGA A	GCT CGA A 1020 GCT CGA	CAC V AAA TTT K	AAA TTT K GCT CGA	GAG CTC E 103 ATT TAA I	GTT CAA V 30 GGT CCA	GAA CTT E AAA TTT K	GCG CGC A 1(	TTG AAC L 040 ATA TAT I	GAC L CAC GTG	TCA AGT S CAA GTT	TCT AGA S 1050 AAT TTA N	TAT I AAT TTA	CTA D> GGT CCA
10	CAA V 010 GAA CTT E	AAT L ATT TAA I	CTT GAA L GCT CGA A	GCT CGA A 1020 GCT CGA A	AAA TTT K	AAA TTT K GCT CGA A	GAG CTC E 101 ATT TAA I	GTT CAA V 30 GGT CCA G	GAA CTT E AAA TTT K	GCG CGC A 10 AAA TTT .K	TTG AAC L 040 ATA TAT I	CAC GTG H	TCA AGT S CAA GTT	TCT AGA S 1050 AAT TTA N	TAT I AAT ATT A N 00	CTA D> GGT CCA G>
10	CAA V 010 GAA CTT E 100	AAT L ATT TAA I GAT	CTT GAA L GCT CGA A	GCT CGA A 1020 GCT CGA A	AAA TTT K	AAA TTT K GCT CGA A	GAG CTC E 103 ATT TAA I	GTT CAA V 30 GGT CCA G	GAA CTT E AAA TTT .K	GCG CGC A 10 AAA TTT .K	TTG AAC L O40 . ATA TAT I 105	CAC GTG H	TCA AGT S CAA GTT Q	TCT AGA S 1050 AAT TTA N 11	TAT I TAA TAA ATT	CTA D> GGT CCA G> TAT
10	CAA V 10 GAA CTT E 100	AAT L ATT TAA I GAT CTA	CTT GAA L GCT CGA A	GCT CGA A 1020 GCT CGA A 10 GAA CTT	AAA TTT K	AAA TTT K GCT CGA A AAT TTA	GAG CTC E 103 ATT TAA I CAC GTG	GTT CAA V 30 GGT CCA G 1080	GAA CTT E AAA TTT .K	GCG CGC A 10 AAA TTT .K TCA AGT	TTG AAC L 105	CAC GTG H TTA AAT	TCA AGT S CAA GTT Q GCG CGC	TCT AGA S 1050 AAT TTA N 11 GGA CCT	AAT TTA N	CTA D> GGT CCA G> TAT ATA
10	CAA V 10 GAA CTT E 100 TTG AAC L	AAT L ATT TAA I GAT CTA D	CTT GAA L GCT CGA A ACC TGG	GCT CGA A 1020 GCT CGA A 10 GAA CTT	CAC V AAA TTT K D70 TAT ATA Y	AAA TTT K GCT CGA A AAT TTA	GAG CTC E 103 ATT TAA I CAC GTG H	GTT CAA V 30 GGT CCA G 1080 AAT TTA	GAA CTT E AAA TTT .K GGA CCT	GCG CGC A 10 AAA TTT .K TCA AGT S	TTG AAC L )40 ATA TAT 109 TTG AAC L	CAC GTG H TTA AAT L	TCA AGT S CAA GTT Q GCG CGC	TCT AGA S LOSO AAT TTA N 11 GGA CCT G	AAT TTA N CGT GCA R	CTA D>  GGT CCA G>  TAT ATA Y>
10	CAA V 10 GAA CTT E 10 TTG AAC L	AAT L ATT TAA I GAT CTA	CTT GAA L GCT CGA A ACC TGG	GCT CGA A 1020 GCT CGA A 10 GAA CTT	CAC V  AAA TTT K  O70 TAT ATA Y  11:	AAA TTT K GCT CGA A AAT TTA N	GAG CTC E 103 ATT TAA I CAC GTG H	GTT CAA V 30 GGT CCA G 1080 AAT TTA	GAA CTT E AAA TTT .K GGA CCT	GCG CGC A 10 AAA TTT .K TCA AGT S	TTG AAC L O40 ATA TAT I 109 TTG AAC L	CAC GTG H TTA AAT	TCA AGT S CAA GTT Q GCG CGC	TCT AGA S LOSO AAT TTA N 11 GGA CCT G	AAT TTA N CGT GCA R	CTA D>  GGT CCA G>  TAT ATA Y>
10	CAA V 10 GAA CTT E 10 TTG AAC L	AAT L ATT TAA I GAT CTA D	CTT GAA L GCT CGA A ACC TGG	GCT CGA A 1020 GCT CGA A 10 GAA CTT E	AAA TTT K D70 TAT ATA Y	AAA TTT K GCT CGA A AAT TTA N	GAG CTC E 103 ATT TAA I CAC GTG H	GTT CAA V 30 GGT CCA G 1080 AAT TTA N	GAA CTT E AAA TTT K GGA CCT G	GCG CGC A 10 AAA TTT K TCA AGT S	TTG AAC L )40 ATA TAT I 105 TTG AAC L	CAC GTG H TTA AAT L	TCA AGT S CAA GTT Q GCG CGC A	TCT AGA S LOSO AAT TTA N 11 GGA CCT G	AAT TTA N CGT GCA R	CTA D> GGT CCA G> TAT ATA Y>
10	CAA V 10 GAA CTT E 10 TTG AAC L GCA CGT	AAT L ATT TAA I GAT CTA D 1110 ATA TAT	CTT GAA L GCT CGA A ACC TGG T	GCT CGA A 1020 GCT CGA A 10 GAA CTT E	CAC V  AAA TTT K  70 TAT ATA Y  11: CTA GAT	AAA TTT K GCT CGA A AAT TTA N	GAG CTC E 103 ATT TAA I CAC GTG H	GTT CAA V 30 GGT CCA G 1080 AAT TTA N	GAA CTT E AAA TTT K GGA CCT G	GCG CGC A 11 AAA TTT K TCA AGT S	TTG AAC L 105 AAC L GAT CTA	CAC GTG H TTA AAT L 1140 GGA CCT	TCA AGT S CAA GTT Q GCG CGC A	TCT AGA S 050 AAT TTA N 11 GGA CCT G	AAT TTA N CGT GCA R	CTA D> GGT CCA G> TAT ATA Y> GAA CTT

FIGURE 37 (3 of 5)

Osp b/ fla (122-234) osp c 1180 1190 1200 1160 1170 • GGA TTA AAG GAA AAA ATT GAT GCG GCT AAG AAA TGT TCT GAA ACA TTT CCT AAT TTC CTT TTT TAA CTA CGC CGA TTC TTT ACA AGA CTT TGT AAA G L K E K I D A A K K C S E T F> 1220 1210 1230 ACT AAT AAA TTA AAA GAA AAA CAC ACA GAT CTT GGT AAA GAA GGT GTT TGA TTA TTT AAT TTT CTT TTT GTG TGT CTA-GAA-CCA TTT CTT CCA CAA TNKLKEKHTDLGKEG V> 1250 1260 1270 1280 ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA AAA ACA AAT GGT ACT AAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT TTT TGT TTA CCA TGA TTT D A D A K E A I L K T N G T K> 1310 1320 1300 1330 ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TTT GAA TCA GTA GAG GTC TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT AAA CTT AGT CAT CTC CAG T K G A E E L G K L F E S V E V> 1360 1370 1380 1350 TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAT TCA GTT AAA GAG CTT AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA TTA AGT CAA TTT CTC GAA L S K A A K E M L A N S V K E L> 1430 1400 1410 1420 ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA AAA CCT GGT ACC ATG GCT TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT TTT GGA CCA TGG TAC CGA T S P V V A E S P K K P G T H A> 1450 1460 1470 1480 CAA TAT AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TCT CAA AAT GTT ATA TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA AGA GTT TTA Q Y N Q M H M L S N K S A S Q N> 1490 1500 1510 1520 GTA AGA ACA GCT GAA GAG CTT GGA ATG CAG CCT GCA AAA ATT AAC ACA

CAT TCT TGT CGA CTT CTC GAA CCT TAC GTC GGA CGT TTT TAA TTG TGT V R T A E E L G M Q P A K I N T>

Osp b/ fla (122-234) osp c

	15	40		15	550		:	1560			15	70		1	580	
		•	•		•		•	•		.*		•	•		•	
	CCA	GCA	TCA	CTT	TCA	GGG	CTT	CAA	GCG	TCT	TGG	ACT	TTA	AGA	GTT	CAT
												TGA				
												T				
	•															•••
		1590	•		160	00		16	510		:	1620			16	30
•	• ,,,	•		•		•	•	•	•	*1	•	•		•		•
	GTT	GGA	GCA	ACC	CAA	GAT	GAA	GCT	ATT	GCT	GTA	AAT	ATT	TAT	GCA	GCT
												TTA				
		G		T								้ท		Y	λ	
					_							-	-	•	••	• • • •
		1	540		•	1650			166	50		16	570			1680
	•		•		•	• .		•		•	•		•		•	•
	AAT	GTT	GCA	AAT	CTT	TTC	TCT	GGT	GAG	GGA	GCT	CAA	ACT	GCT	CAG	GCT
												GTT				
	N		A									Q			0	
	• •												_			
			169	90		17	700		1	710			172	0.0		
		•		•	•		•		•	•		•		*	•	
	GCA	CCG	GTT	CAA	GAG	GGT	GTT	CAA	CAG	GAA	GGA	GCT	CAA	CAG	CCA	GCA
												CGA				
												A				
				-				_	_				•	w.	•	
17	730		. 3	1740			175	50		17	760					-
	•		•	•,		•		• .	•		•		•			
	CCT	GCT	ACA	GCA	CCT	TCT	CAA	GGC	GGA	GTT	GGT	CAC	С			
												GTG	_			
			T						G			Н	_			

FIGURE 37 (5 of 5)

		•	10	•		20			30		*		40	*	
OspC-B31	ATG A	AA AAC	AAT	ACA TGT	TTA AAT	AGT	GCG	ATA	TTA	ATG	ACT	TTA AAT	TTT AAA	TTA AAT	TTT AAA
1. OspC-P	к •••••	•• ••	10		•••	20	• • •	• • •	30	•••	• • •	•••	40	•••	>
2. OspC-T	R		10			20	•••		30	•••		•••	40		>
3. Ospc-K	4	• • • • •	10		•••	20		•••	30				40	•••	>
	50		60			•	70			80		*	90		*
OspC-B31	ATA T	CT TGT	TAA	TAA	TCA	GGG	AAA	GAT	GGG	AAT TTA	ACA TGT tgc	TCT	GCA	AAT	TCT
1. OspC-P: [ 1832 ]	K50	• • • •	60 • g •	•••		• • •	70 •••	.g.	• • •		Ţ	90	a.t	•••	c>
2. OspC-T		••••													
3. Ospc-K	450		60			-	70				80			9	90
·•	100		3	110			120			13	30 ·			L <b>4</b> 0	
OspC-B31		AT GAC	TCT	GTT	AAA TTT	CCC	CCT	AAT	CTT	ACA	GAA	ATA	AGT	* AAA TTT	AAA TTT
1. OspC-1	00	.c	110	.cg	•••	120	•••		13	30	•••			•••	>
2. OspC-T	R 		.00	.ca	:	110 a	•••		120	c	'.t.	13		• • •	>
3. Ospc-K	⁴		.00	.ca	:	a	•••	•••	120	•••	.t.	13		• • •	>
	* 1	.50	*	16	50	*	3	L70 *		*	180		*	19	0
OspC-B31	ATT A	CG GAT	TCT	TAA TTA	CCC	GTT CAA	ATT TAA	CTT GAA	GCT.	GTG	AAA	GAG	GTT CAA	GAA CTT	GCG CGC
1. OspC-P: [ 1832 ]		.a			a		9	•••	•••	180 t	•••	а	19		a.t>
2. OspC-T	140	.a	150		a	t	50	g	•••	170	•••	a	180	g	t>
3. OspC-K [ 1774 ]	140	.a	150	• • •	a	t	g	g	<u>.</u>		•••	a	180	g	t>
	*	200		*	210	,	*	22	20		2	230		*	240
OspC-B31	TTG C		TCT AGA	ATA'	GAT	GAA	ATT	GCT	GCT	AAA	GCT	ATT	GGT	AAA	AAA
1. OspC-P	K 20	00 J.t .t	• • •	210	•••	•••	c22	20	aag	2	30	•••		240	>
2. OspC-T [ 1786 ]							210			•••	22	20			230

Figure 38 (1 of 3)

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													•			
3. OspC-1	K4 19	0			200			210			2	20			230	
[ 1//4 ]	• • •	a.c	• • •	• • •	• • •	• • •	• • •	c	• • •	aa.	• • •	• • •	• • •	• • •	• • •	gt.>
			2.	50		:	260			270			2	80		
		*		*	*		*		*	*		*		*	*	
OspC-B31	TAT TAT	CAC	CAA	AAT	TAA	GGT	TTG	GAT	ACC	GAA	TAT	AAT	CAC	AAT	GGA	TCA
•																
1. OspC-1 [ 1832 ]	PK	25	50		:	260			270			. 2	80			290
[ 1832 ]		g	a.t		• • •	• • •	a	.c.	g.t	tt.	a	•••	g		• • •	g>
													_			•
						tac										
2. Ospc-1 [ 1786 ]	איי			240		ا و ا	50			260			270			•
[ 1786 ]	• • •				g		a		.a.		gca		.ga		.a.	>
3. OspC-1 [ 1774 ]	(4	240			2	50		:	260		•	270			2	80
[ 1//4 ]	• • •	t	• • •	• • •	• • •	• • •	a	a	g.t	a.t	gcg	gg.	a		• • •	>
	290 *			300			3	10			320			- 330		
	*		*	*		*		*	*	•	*		*	*		*
OspC-B31	TTG	TTA	GCG	GGA	CGT	TAT	GCA	ATA	TCA	ACC	CTA	ATA	AAA	CAA	AAA	TTA
1. OspC-F [ 1832 ]	ĸ		300			3:	10			320			330			
[ 1832 ]			a		gcc		• • •			• • •			.c.	g.,		
2 0																-
2. OspC-2 [ 1786 ]	80	_		290			300			. 3:	LO			320		_
[ 1,00 ]	• • •	a	· · d	• • •	ge.	• • •	.a.	• • •	• • •	.aa	• • •	• • •		• • •	• • •	>
3. OspC-X	4	2	90			300			3:	10		2	320			330
[ 1774 ]			a		gcc							• • •	.c.	g		>
														-		
	34	0			350			360			2*	, o			200	
	. 34	0	*	:	350		*	360	·	*	37	70 *	*	:	380	
OspC-B31	GAT	O * GGA	* TTG	AAA	350 * AAT	GAA	* GGA	360 *	AAG	* GAA	37 AAA	70 * ATT:	* GAT	GCG	380 * GCT	AAG
OspC-B31	GAT CTA	0 * GGA CCT	* TTG AAC	AAA TTT	AAT TTA	GAA CTT	* GGA CCT	360 * TTA AAT	AAG TTC	GAA CTT	37 AAA TTT	O * ATT	¢ GAT CTA	ece cec	380 * GCT CGA	AAG TTC
OspC-B31	GAT (	gga CCT	TTG AAC	AAA TTT	AAT	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT. TAA	GAT CTA	GCG CGC	GCT CGA	AAG TTC
OspC-B31	GAT (	gga CCT	TTG AAC	AAA TTT	AAT	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT. TAA	GAT CTA	GCG CGC	GCT CGA	AAG TTC
OspC-B31	GAT (	gga CCT	TTG AAC	AAA TTT	AAT	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT. TAA	GAT CTA	GCG CGC	GCT CGA	AAG TTC 390
1. OspC-3 [ 1832 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT TAA	GAT CTA 880	GCG CGC	GCT CGA	390
1. OspC-3 [ 1832 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT TAA	GAT CTA 880	GCG CGC	GCT CGA	390
OspC-B31	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT TAA	GAT CTA 880	GCG CGC	GCT CGA	390
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA (ACC) (CTA (A	GGA CCT aa.	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT TAA	GAT CTA 80 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA (ACC) (CTA (A	GGA CCT aa.	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT TAA	GAT CTA 80 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA (ACC) (CTA (A	GGA CCT aa.	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT 360	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT TAA	GAT CTA 80 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ]	GAT (CTA (ACC) (CTA (A	GGA CCT aa.	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT 360	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT TAA	GAT CTA 80 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA) 40 ag. (R330) ag.	aa. .t.	TTG AAC	AAA TTT 350 	AAT TTA ttt a 10 tca ttc	360 	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT TAA	GAT CTA 80 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ]	GAT (CTA) 40 ag. (R330) ag.	aa. .t.	TTG AAC	AAA TTT 350 	AAT TTA ttt a 10 tca ttc	360 	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT 9 360	ATT TAA	GAT CTA 380 .ca a.a	GCG CGC	GCT CGA	390 > >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K	GAT (CTA (40 ag. 4 ag. 4	aa. .t.	TTG AAC	AAA TTT 350	AAT TTA ttt a 10 tca ttc	360 	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac. a	AAA TTT 360	37 	GAT CTA 380 .ca a.a	aa. 37.a.	GCT CGA	390 > >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ]	GAT (CTA (ACTA (AC	GGA CCT aa. .t.	TTG AAC	AAA TTT 350 t	AATTTA ttt .a 10 tca ttca 40 ACA	360   50 	GGA CCT	TTA AAT	AAG TTC 350 	GAA CTT 70 ac. a	AAA TTT 360	37 420	GAT CTA 380 .ca a.a	aa. 37.a.	GCT CGA	390 > >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ]	GAT CTA 40 ag. 4 ag. 4 AAA 7 TTT 1	aa. .t.	TTG AAC	AAA TTT 350 t	AAT TTA ttt a 10 ca ttc a 40 ACA TGT	GAA CTT 360  50 *TTT AAA	GGA CCT	AAT TTA	AAG TTC 3: 360 t	GAA CTT 70 ac. a	AAA TTT 360 	ATT TAA 37 420 GAA CTT	GAT CTA 880 .ca a.a a	aa. 37.a. .a.	GCT CGA	390 > >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P	GAT CTA 40 ag. 4 ag. 4 AAA 7 TTT 1	aa. .t.	TTG AAC	AAA TTT 350 34 GAA CTT	AAT TTA ttt a 10 tca ttc	GAA CTT 360 	GGA CCT	AAT TTA	AAG TTC 360 t	GAA CTT 70 ac. a TTA AAT	AAA TTT 360 	ATT TAA 37	GAT CTA 380 .ca a.a 70 a	aa. 37.a.	GCT CGA	390> 380> 380> 380>
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P	GAT CTA 40 ag. 4 ag. 4 AAA 7 TTT 1	aa. .t.	TTG AAC	AAA TTT 350 34 GAA CTT	AAT TTA ttt a 10 tca ttc	GAA CTT 360 	GGA CCT	AAT TTA	AAG TTC 360 t	GAA CTT 70 ac. a TTA AAT	AAA TTT 360 	ATT TAA 37	GAT CTA 380 .ca a.a 70 a	aa. 37.a.	GCT CGA	390> 380> 380> 380>
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ]	GAT CTA 40 ag. R330 ag. 4 ag. FTTT 1	GGA CCT aa. .t. aa. 390* TACA	TCT AGA	AAA TTT 350 t 360 t	AATATTA tttt a lo ca ttc a 40 ACATGT ga.	GAA CTT 360  50 * TTT AAA	.a. .a. .ag	AAT TTA	AAG TTC 3 360 t	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 420 GAA CTT agt	GAT CTA 380 .ca a.a 70 .a AAA TTT 43	aa. 37.a. .a. CACGTG	GCT CGA	390> 380> 380> 380>
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T	GAT CTA 40 ag. R330 ag. 4 ag. RAAR TTT I	GGA CC aa. .t. aa. 390*TACA	TTG AAC	AAA TTT 350 34 t	AATA TTA ttt .a 10 ca ttc .a 40 ACA TGT ga.	GAA CTT 360  50 *TTT AAA	.a. .ag .ACT	AAT TTA	360 t	GAA CTT 70 ac. a TTA AAT 420 C	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt	GAT CTA 380 .ca a.a 70 .a AAA TTT 43	aa. 37.a. .a. CACGTG	GCT CGA	390 > > 880 > GAT CTA
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA 40 ag. R330 ag. 4 ag. R34 TTT 1	GGA CCT aa. .t. aa. 390 TGA ACA	TTG AAC	AAA TTT 350 t	AATA  TTA  ttt  a loca ttc  ACA TGT  ga. 390 a.	GAA CTT 360 	aaag ACT TGA	AAT TTA	AAG TTC 3 360 t	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t	GAT CTA 80 .ca a.a 0a AAA TTT 43 ggt	ccc ccc aa. 37. a. cac cctc	GCT CGA 70 43 ACA TGT 420 g	390> 880> GAT CTA>
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA 40 ag. R330 ag. 4 ag. R34 TTT 1	GGA CCT aa. .t. aa. 390 TGA ACA	TTG AAC	AAA TTT 350 t	AATA  TTA  ttt  a loca ttc  ACA TGT  ga. 390 a.	GAA CTT 360 	aaag ACT TGA	AAT TTA	AAG TTC 3 360 t	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t	GAT CTA 80 .ca a.a 0a AAA TTT 43 ggt	ccc ccc aa. 37. a. cac cctc	GCT CGA 70 43 ACA TGT 420 g	390 > > 880 > GAT CTA
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA 40 ag. R330 ag. 4 ag. R34 TTT 1	GGA CCT aa. .t. aa. 390 TGA ACA	TTG AAC	AAA TTT 350 t	AATA  TTA  ttt  a loca ttc  ACA TGT  ga. 390 a.	GAA CTT 360 	aaag ACT TGA	AAT TTA	AAG TTC 3 360 t	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t	GAT CTA 80 .ca a.a 0a AAA TTT 43 ggt	ccc ccc aa. 37. a. cac cctc	GCT CGA 70 43 ACA TGT 420 g	390> 880> GAT CTA>
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T	GAT CTA 40 ag. R330 ag. 4 ag. R34 TTT 1	GGA CCT aa. .t. aa. 390 TGA ACA	TTG AAC	AAA TTT 350 t	AATA  TTA  ttt  a loca ttc  ACA TGT  ga. 390 a.	GAA CTT 360 	aaag ACT TGA	AAT TTA	AAG TTC 3 360 t	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t	GAT CTA 80 .ca a.a 0a AAA TTT 43 ggt	ccc ccc aa. 37. a. cac cctc	GCT CGA 70 43 ACA TGT 420 g	390 > > 880 > GAT CTA
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA 40 ag. R330 ag. 4 ag. R34 TTT 1	GGA CC aa. .t. aa. 90 * TACA 	TTG AAC	AAA TTT 350 t	ATTA  OCA  CA  TGT  Ga.  390.	GAA CTT 360 	aaag ACT TGA	AAT TTA	360  360  10 AAA TTT	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t .gt	GAT CTA 80 .ca a.a 0a AAA TTT 43 ggt	ccc ccc aa. 37. a. cac cctc	GCT CGA 70 43 ACA TGT 420 g	390 > > 880 > GAT CTA

Figure 38 (2 of 3)

OspC-B31 CTT GGAA C	GT AAA GAA GGT GTT CA TTT CTT CCA CAA	ACT GAT GCT GAT	GCA AAA GAA GCC ATT TTA CGT TTT CTT CGG TAA AAT
1. OspC-P440 [ 1832 ]	450 .c c.g .ac.	460	470 480
2. OspC-TR [ 1786 ]	430 440t. c a.c	450 caga. a	460 470 at >
			60 470
		•	520 * * *
OBPC-B31 AAA AC	CA AAT GGT ACT AAA	ACT AAA GGT GCT	GAA GAA CTT GGA AAA TTA CTT CTT GAA CCT TTT AAT
	•		520 530 a t aa. g.t>
			510 a a. g.g>
			510 520 a>
530	540	550	560 570 * * * *
OspC-B31 TTT GA AAA CI	* * * * * * * * * * * * * * * * * * *	TTG TCA AAA GCA AAC AGT TTT CGT	* * * * * GCT AAA GAG ATG CTT GCT CGA TTT CTC TAC GAA CGA
1. OspC-PK 54 [ 1832 ]	550a .gt	560	570 580 cta gcaa a>
2. OspC-520 [ 1786 ] a.	530 ca ag.	540 55	50 560 g cca gca t.a a>
3. ОврС-K4 530 [ 1774 ] .с	540 • • • • a ag.	550 g	560 570 g ca gca t.a>
			610 620
OSPC-B31 AAT TO	A GTT AAA GAG CTT T CAA TTT CTC GAA	ACA AGC CCT GTT TGT TCG GGA CAA	GTG GCA GAA AGT CCA AAA CAC CGT CTT TCA GGT TTT
1. OspC-PK [ 1832 ]	590 600	610	620 630 a>
2. OspC-TR570 [ 1786 ]	580	590	600 610>
3. OspC-K4 [ 1774 ]	580 590	600	610 620
63	0		
OspC-B31 AAA CC	* T TAA A ATT		•
1. OspC-PK [ 1832 ]	•,•••>		
2. OspC-TR 620 [ 1786 ]	>	•	· .
3. OspC-K4 [ 1774 ]	630	-	•

Figure 38 (3 of 3) SUBSTITUTE SHEET (RULE 26)

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									/ \	, , ,	33						
					10			20			30 *			-	40		
. B	Oggo Os						TTT	TTA	TTG	CTC	TCA	ATA					GAT CTA
																MAT	CTA
Į	1. P-Gau 2804 ]	• • • •	• • •	• • •	10			20	• • •	•••	30	• • •	•••	- •.••	40 .a.	•••	>
	2. DK29 o	8			10			20			30				40		
Ţ	2. DK29 of 2786 ]	• • •	• • •	c	• • •	• • •	•, • •	• • •	• • •	• • •	• • •	• • •	• • •	g.,	• • •	• • •	>
	3. K48 os				10			20			30				40		
[	2786 ]	• • •	• • •	• • •	• • •	• • •	• • •	• • •	•••	• • •	• • •	• • •	• • •	• • •	• • •	• • •	>
						•							•			•	
		50 *		*	60 *		*	•	70 *	*		80			90		•
В	O ospD	AAT	GAA	GGT	GTA	AAC	TCA	AAA	GAT	TAC	GAG	TCA	AAA	AAA	CAG	AGT TCA	ATA TAT
	1. P-Gau	50			60			•	70			80			90		
Ι	2804 }	• • •	• • •		60	• • •	• • •	• • •	• • •	• • •	• • •	•••	• • •	• • •	•••		>
	2. DK29 OF	<b>s</b> 50			. 60		•	-	70			80			90		
I	2786 ]	• • •	• • •	• • •	• • •	• • •	• • •	• • •		• • •	• • •	• • •	• • •	• • •		• • •	>
	3. K48 osp 2786 ]	50			60	-			70			80			9.0		
ĺ	2786 ]	• • •	• • •	• • •	• • •	·g·	• • •	•••	• • •	• • •	•••	• • •	• • •	• • •		• • •	•••>
	•																200
	: .	10	00 *		3	110 *		*	120		*	13	\$0 *		•	140	
B	O ospD .	CTA GAT	GGT CCA	GAA CTT	TTA AAT	AAT TTA	CAG GTC	CTA GAT	TTG AAC	GGG CCC	CAA GTT	ACT TGA	ACA TGT	AAT TTA	TCA AGT	CTA GAT	AAA TTT
	1. P-Gau	10	00		3	.10			120			13	0		:	L40	
ſ	1. P-Gau c 2804 J	• • •	• • •	• • •	• • •	•••	• • •	•••	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	>
	2. DK29 os 2786 ]	10	00		1	.10			120			13	0		1	40	
Į	2786 ]	•••	• • •	• • •	••••	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	>
	3. K48 osp	10	00		1	10			120			13				40	
L	2786 ]	•	•••	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• *• •	• • •	• • •	• • •	>
-			150			16	n'			70	. · ·	-		· •			
		*	*		*	10	o . *	*	1	*		*	*		*	19	-
. BC	O cspD	GAA CTT	GCA CGT	AAA TTT	AAT TTA	ACA TGT	ACA TGT	GAT CTA	AAT TTA	TTA AAT	AAT ATT	GCA CGT	TCA AGT	TAA TTA	GAG CTC	GCA CGT	aat Tta
_	1. P-Gau o	*	150			16	0		1	70			180			19	0
I	2804 }	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• '• •	• • •	•••	• • •	• • •	•••>
I	2. DK29 os 2786 ]	• • •	150		• • •	16	o • • •	• • •	1	70			180		• • •	19	
	3. K48 osp	,	150			16	o ·		1	70			180			19	0
I	2786 j	•••	•••	• • •	•••			• • •			• • •			•••	•••	•••	
			2	200			210		-	22	0		9	30			240
Þr	) ospD	*	C MITT	*	C 2 2	*	*	3 M S	*		0 *	*	<u>-</u>	*		*	*
٥	, ospu	TTT	CAA	CAT	GAA CTT	CGT	CAA	TAT	TCA	CAC	CAA	TTA	ATT TAA	TAA TAA	TCA AGT	TCT AGA	gct Cga

-	•				96/13	3		
1. P-Gau [ 2804 ]	0	200	210	· · · · · · · · · · · · · · · · · · ·	220	 · •••, •••	230	240
2. DK29 [ 2786 ]		200	210	•	220		230	240
3. K48 o	sp	200	210		220		230	240
[ 2786 ]	•••	,		• • • • • •	• • • • • •	• • • • • •	••• •••	>
	*	250 *	*	260	270 * *			*
BO ospD	GCA GAT CGT CTA	CAG GTA	AAA GG1	CAA CAA GTT GTT	CAA ATA	TGC ACG	ATT TAG (	CTC AAA CAG TTT
1. P-Gau [ 2804 ]		250		260	270		280	
2. DK29		250 ••••g			270	1	280	
3. K48 o	<b>S</b> D	250		260	270		280	
[ 2786 ]	•••	••• ••g	•••	•••	• • • • • •		• • • • • •	>
		* *	*	310	* .	320 *	330 * *	*
BO ospD	TGG CAG ACC GTC	AAA TAG	TAA ATC	AAA AAA TTT TTT	TAA AGG ATT TCC	AAT CTA TTA GAT	GTG ATA A	AG TAA TC ATT
1. P-Gau [ 2804 ]		300		310		320	330	>
2. DK29 (	290	300	•••	310	•••	320	330	
3. K48 o	<b>3290</b>	300		310		320	330	•• •••
[ 2700 ]			•••		•••	•••	••• ••• •	>
PO ocah	340 *	*	350	360	*		38	*
BO ospD	ATC AAC	GCC GAT	TAC AAC	GCT TTC	AAG CAT TTC GTA	ATA ACC	TTA CTA A AAT GAT T	AG CAG TC GTC
1. P-Gau [ 2804 ]	0 340	•••	350 .*** ***	360	•••	370	38	0
2. DK29 6	эв 340	•••	350	360	•••	370	38	0
3. K48 of	sp 340	,	350	360		370	38	0
,,		. *		•••	•••	•••		>
BO ospD	390 * *	*	400 *	*	410	420	*	430 *
_	ATC TTG	TTT TAT	ACG TTT	TTG ACA	ACA AAG TGT TTC	AGC AAG TCG TTC	AAG AGC A	AC TAA TG ATT
1. P-Gau [ 2804 ]	390	•••	400	•••	410	420	•••	430
2. DK29 d	s 390		400		410	420		430

Figure 39 (2 of 4)
SUBSTITUTE SHEET (RULE 26)

	I	2786	3	• •								97/	1133						
														•••	••••	• •	••••	• • •	• •••>
	[	3. K4 2786	)	 		• • •			400 • • •			410	) 		42	20			430
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						440	•		45	0			460			470	)		480 *
	ВС	Ospi	)	AA	T AC	* TAT	C TG	* A TT(	C TG	* A TC	≄ מממ.	י אר אה	* ממני	יר אר	*			*	AAA I
				TT	G TG	A TA	G AC	T AAC	G AC	T AC	T TI	G TC	T TO	C TO	AA AS	G AC	T AC	A AA' I TT	T AAA A TTT
	,	1. P-	Gau	0	W.	440			45	0.			460	•		470	)		480
	ι	2504	1	• •	• • •	• ••	• • • •	• • • •	• • •	• • •	• ••	• • •	• ••		• • •	•	• ••		>
	r	2. DK 2786	29	08		440			45	0			460			470			480.
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	1	3. K4 2786	8 o 1	sp		440			45	0			460			470		•	480
	•		•			• • • •	• • • •	•••	• • • ·	• • • •	• • • 9	• • •	• ••	• • •	• • • •	• • •	• • • •	•••	>
						4	190			500				· `					
	ВО	OggD		ACI	*		*	*		*		*	21	<b>∪</b> .	*	• ;	520 *	*	•
		OspD		TGI	TCG	ATI											C AGT		AGT
	:	1. P-0	Gau	0															ICA
		2804		• • •	• • •	• • •	• • •	• • •	• • •	• • • •		• • •			• • • •	• • •	20		>
	. :	2. DK2 2786	29 (	ac		4	90			500			510	)			:20		
	l 4	2/86	j	• • •	• • •	•••	• • •	• • •	• • •	• • •	• • •	• • • •	• • • •	•••	• • •	• • •	• • • •	•••	>
1	3 1 2	3. K48 2786 ]	3 os	₽,		4	90			500		•	510	)		. 5	20		
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				530			540			E	<b>E</b> 0							•	
E	30	ago	٠	530 *		*	*		*	. 5	*	*	-	560		*	570 *		*
		OspD															GGC	ATT	GGA
	1	. P-G	au	530			540			F.					GII	101	فانانا	TAA	CCT
[	2	• P-G 804 ]			• • •	• • •	• • • •	• • •		• • •	•••	• • •		560			570		_
	2	. DK2	9 0	530			E 40												
Į	2	786 ]		• • •	• • •	• • •	• • •	• • •	• • •	• • • •	•••	• • •	• • •	•••	• • •		570		>
	3	. K48 786 j	os	530			540			55				560			570		
ı	_	,00 ]		• • •	• • •	•••	• • •	• • •		•••	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	>
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ъ,	<u> </u>				*	*		90 *		•	600		*	61	LO *	•		20	
Þ	<b>U</b> (	Ogac		AAT ATT	AAT TTA	AAA TTT	GAC .	AGA . TCT	AAC	CGC	GAA	~~~			_	TAC	AGA '	TAT .	AGA
	1.	. P-Ga	911 /			<b>-</b>			~ + •	000	<b>C</b> 11	GII	ATG	TTT	TGA	ATG	AGA TOT	ATA	TCT
I	28	304 ]	(	•••	• • •	• • •	5	90	• • •	• • •	600	• • •		61	0		6	20	
	2.	DK29	9 09	58	0			90		•	coo	- · ·	•••	• • •	- • •	• • •	• • •	• • •	>
[	27	786 ]		• • •	• • •	• • •	•••	•••	• • •	• • •	600			61	0		62	20	
	3.	K48	osi	58	0		59	90			600			· · ·	^	- • •	•••		• • • >
ſ	27	786 j		• • •	• • •	• • •	•••		• • •	•••		• • •	• • •	61	• • •		62	20	>

									9	8/1	<i>33</i>						
		630			64	40		(	650			660		_		70	
BO ospD	* AGA	AGT	AGC	* AGA	GTT	* AGT	ATT	ACA	GAT	AGC	CAA	AAA	TGT	AGC	GGA	AAT	
	TCT	TCA	TCG	TCT	CAA	TCA	TAA	TGT	CTA	TCG	GTT	TTT	ACA	TCG	CCT	TTA	
1. P-Gau	0	630			64	40		(	650		-	660		-	67	70	
[ 2804 ]	• • •	• • •	•••	• • •	• • •	• • •	• • •	• • •	a	• • •	• • •	• • •	• • •	• • •	• • •	>	
2. DK29 o					64							660			67	70	
[ 2786 ]	• • •	• • •	• • •	• • •	• • •		•••	• • •	a	• • •	• • •	• • •	•••	• • •	• • •	>	
3. K48 os	P	630			64	40			650			660		,		70	
[ 2755 ]	•••	• • •	•••	•••	•••	•••	•••	•••				•••	•••	• • •	•••	• • • •	
	ē		580			690		•	71	00							
	*		*		*	*		*		*		*	-			- '	
BO ospD										TAC ATG							
1. P-Gau	0		680			690	4.		76	00							
[ 2804 ]	• • •	• • •	• • •	• • •	• • •	• • •	• • •	•••	• • •	• • •	>						
2. DK29 o	s		680			690			·· 70	00							
[ 2786 ]	• • •	• • •	• • •	• • •	•••	• • •	• • •	• • •	• • •	• • •	>						
3. K48 os						690				00	_	•					
[ 2786 ]	• • •	• • •	• • •		• • •	• • •	• • •	• • •	• • •	• • •	>						

P41 .				
Sequence	Range:	1	to	1011

		1	.0			20			30			4	40		
	÷		•	•		•		•	•		•		•	•	
															AAT
															TTA
Met	Ile	Ile	Asn	His	Asn	Thr	Ser	Ala	Ile	Asn	Ala	Ser	Arg	Asn	Asn>
50			60			-	70			80			90		-
•		•	*		•	·	•	•		•		•	•		•
GGC	ATT	AAC	GCT	GCT	AAT	CTT	AGT '	AAA	ACT	CAA	GAA	AAG	CTT	TCT	AGT
															TCA
															Ser>
							• • • •			•					
10	0		. 1	110		•	120			1.5	30		•	140	
	The C	N ← N	TTA	እስጥ ስ	CGA	درس. -	<b>дСц</b> . 	CAT	CAT	CCT	ر المان م	eec.	איזיר	CCA	~m~
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•	150			16	50	•	3	.70			180			19	€0
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			ATT												
			TAA												
Ser	Gly	Lys	Ile	Asn	Ala	Gln	Ile	Arg	Gly	Leu	Ser	Gln	Ala	Ser-	λrg>
	:	200			210			22	20		2	230			240
•		•		•	•		. •		•	•		•		•	•
AAT	ACT	TCA	AAG	GCT	ATT	TAA	TTT	ATT	ÇAG	ACA	ACA	GAA	GGG	AAT	TTA
			TTC												
Asn	Thr			* 1 -	* 1 -	y co	Phe	71~	$\sim 1 -$	Th	Thr	C1			Leus
		Ser	Lys	MIG	116	N311		116	GIII	1111		GIU	Gly	Asn	
	•			VIG				116	270	1111				Asn	
	•		Lys 50	,		260	,		•	1111	•	28		Asn •	
TAA	•	2!		•	7	260		•	270		•	28	30	•	
ATT	GAA CTT	25 GTA CAT	GAA	AAA TTT	GTC CAG	260 TTA	GTA CAT	• AGA TCT	270 ATG TAC	AAG TTC	• GAA CTT	28 TTG AAC	GCA CGT	GTT CAA	CAA GTT
ATT	GAA CTT	25 GTA CAT	GAA	AAA TTT	GTC CAG	260 TTA	GTA CAT	• AGA TCT	270 ATG TAC	AAG TTC	• GAA CTT	28 TTG AAC	GCA CGT	GTT CAA	CAA
ATT	GAA CTT	25 GTA CAT	GAA CTT Glu	AAA TTT	GTC CAG	TTA AAT Leu	GTA CAT Val	• AGA TCT	270 ATG TAC Met	AAG TTC Lys	• GAA CTT	28 TTG AAC	GCA CGT Ala	GTT CAA	CAA GTT
TTA Asn	GAA CTT	25 GTA CAT	GAA	AAA TTT	GTC CAG	TTA AAT Leu	GTA CAT	• AGA TCT	270 ATG TAC Met	AAG TTC	• GAA CTT	28 TTG AAC	GCA CGT	GTT CAA	CAA GTT
TTA Asn 290	GAA CTT Glu	2! GTA CAT Val	GAA CTT Glu	AAA TTT Lys	GTC CAG Val	TTA AAT Leu	GTA CAT Val	AGA TCT Arg	270 ATG TAC Met	AAG TTC Lys	GAA CTT Glu	28 TTG AAC Leu	GCA CGT Ala	GTT CAA Val	CAA GTT Gln>
TTA Asn 290 •	GAA CTT Glu	2! GTA CAT Val	GAA CTT Glu 300	AAA TTT Lys	GTC CAG Val	TTA AAT Leu 31	GTA CAT Val 10	* AGA TCT Arg	270 ATG TAC Met	AAG TTC Lys 320	GAA CTT Glu	TTG AAC Leu TCT	GCA CGT Ala	GTT CAA Val	CAA GTT Gln>
TTA Asn 290 • TCA AGT	GAA CTT Glu GGT CCA	GTA CAT Val	GAA CTT Glu 300 GGC CCG	AAA TTT Lys ACA TGT	GTC CAG Val TAT	TTA AAT Leu  3: TCA AGT	GTA CAT Val  10 GAT CTA	AGA TCT Arg GCA CGT	270 ATG TAC Met	AAG TTC Lys 320 * AGA TCT	GAA CTT Glu GGT CCA	TTG AAC Leu TCT AGA	GCA CGT Ala 330 ATA TAT	GTT CAA Val	CAA GTT Gln>
TTA Asn 290 • TCA AGT Ser	GAA CTT Glu GGT CCA Gly	GTA CAT Val	GAA CTT Glu 300 GGC CCG Gly	AAA TTT Lys ACA TGT Thr	GTC CAG Val TAT	TTA AAT Leu  3: TCA AGT	GTA CAT Val 10 * GAT CTA Asp	AGA TCT Arg GCA CGT	270 ATG TAC Met	AAG TTC Lys 320 * AGA TCT Arg	GAA CTT Glu GGT CCA Gly	TTG AAC Leu TCT AGA	GCA CGT Ala 330 ATA TAT	GTT CAA Val CAA GTT Gln	CAA GTT Gln> * ATT TAA
TTA Asn 290 • TCA AGT Ser	GAA CTT Glu GGT CCA	GTA CAT Val	GAA CTT Glu 300 GGC CCG Gly	AAA TTT Lys ACA TGT	GTC CAG Val TAT	TTA AAT Leu  3: TCA AGT	GTA CAT Val  10 GAT CTA	AGA TCT Arg GCA CGT	270 ATG TAC Met	AAG TTC Lys 320 * AGA TCT Arg	GAA CTT Glu GGT CCA	TTG AAC Leu TCT AGA	GCA CGT Ala 330 ATA TAT	GTT CAA Val	CAA GTT Gln> * ATT TAA
TTA Asn 290 TCA AGT Ser	GAA CTT Glu GGT CCA Gly	GTA CAT Val AAC TTG Asn	GAA CTT Glu 300 GGC CCG Gly	AAA TTT Lys ACA TGT Thr	GTC CAG Val TAT ATA Tyr	TTA AAT Leu  3: TCA AGT Ser	GTA CAT Val 10 * GAT CTA ASP	AGA TCT Arg GCA CGT Ala	270 ATG TAC Met GAC CTG Asp	AAG TTC Lys 320 * AGA TCT Arg	GAA CTT Glu GGT CCA Gly	TTG AAC Leu TCT AGA Ser	GCA CGT Ala 330 ATA TAT	GTT CAA Val	CAA GTT Gln> * ATT TAA
TTA Asn 290 TCA AGT Ser 3	GAA CTT Glu GGT CCA Gly	GTA CAT Val AAC TTG Asn	GAA CTT Glu 300 GGC CCG Gly	AAA TTT Lys ACA TGT Thr	GTC CAG Val TAT ATA TYr	TTA AAT Leu  3: TCA AGT Ser	GTA CAT Val  GAT CTA Asp 360 GAA	AGA TCT Arg GCA CGT Ala	270 ATG TAC Met GAC CTG Asp	AAG TTC Lys 320 AGA TCT Arg	GAA CTT Glu GGT CCA Gly	TTG AAC Leu TCT AGA Ser	GCA CGT Ala 330 ATA TAT Ile	GTT CAA Val	CAA GTT Gln> * ATT TAA Ile>

	390			. 40	00	_	•	410			420			4	30
															AAT
															TTA
GIN	ıyı	WSII		, met	nis	met	Leu	Ser	ASII	LYS	Sei	Ala	Ser	Gin	Asn>
	4	40			450			46	50		4	170			480
• •		*		*	*		•		*	•		•		•	•
										CCT					
Val	TCT	The	Ala	Glu	CIC	LAN	CCI	MAL	GIC	GGA	CGT	TIT	TAA	TTG	TGT Thr>
V G 1	AT 9	1111	,	Gla		Dea	GLY	1766	<b>G111</b>	-10	VIG	Lys	116	ASI	Inr>
	•	49	0	•	5	000		•	510	ب. سد	- :	. 52	20		
CCA	GCA	TCA	CTT	TCA	GGG	CTT	CAA	GCG [*]	TCT	TGG	ACT	TTA	AGA	GTT	CAT
GGT	CGT	AGT	GAA	AGT	CCC	GAA	GTT	CGC	AGA	ACC	TGA	TAA	TCT	CAA	GTA
Pro	Ala	Ser	Leu	Ser	Gly	Leu	Gin	Ala	Ser	Trp	Thr	Leu	Arg	Val	His>
530		_	540			5	50	_	9	560			570		
CTT.	GGA	GCF.	ACC	د ند	ርልጥ	وذي	GCT.	. ב	CCT	GTA	አእጥ	2 mm	<b>.</b>		•
CAA	CCT	CGT	TGG	GTT	CTA	CTT	CGA	TAA	CGA	CAT	TTA	TAL	1M1	CCT	CCA
Val	Gly	Ala	Thr	Glm	Asp	Glu	Ala	Ile	Ala	Val	Asn	Ile	Tyr	Ala	Ala>
											_				-
51	80	•	:	90		•	600		•	61	•		•	20	
TAA	GTT	GCA	AAT	CTT	TTC	TCT	GGT	GAG	GGÀ	GCT	CAA	ACT	GCT	C2.0	GCT
TTA	CAA	CGT	TTA	GAA	AAG	AGA	CCA	CTC	CCT	CGA	GTT	TGA	CGA	GTC	CGA
Asn	Val	Ala	Asn	Leu	Phe	Ser	CJÀ	Glu	Gly	Ala	Gln	Thr	Ala	Gln	Ala>
~	630			. 64	10		6	550		•	660			€7	· <del>-</del> .
•	•		•		•	•		•		•	•		•		•
GCA	CCG	GTT	CAA	GAG	GGT	GTT	CAA	CAG	GAA	GGA	GCT	CAA	CAG	CCA	GCA
CGT	GGC	CAA	GTT	CTC	CCA	CAA	GTT	GTC	CTT	CCT	CGA	GTT	GTC	GGT	CGT
Ala	PIO	vaı	GIN	GIU	GIÀ	vai	Gin	GID	GIU	Gly	Ala	Gln	Gln	Pro	Alax
	(	580		•	690		•	70	00	•	7	710		•	725
CCT	GCT	ACA	GÇA	CCT	TCT	CAA	GGC	GGA	GTT	AAT	TCT	CCT	GTT	AAT	GTT
GGA	CGA	TGT	CGT	GGA	AGA	GTT	CCG	CCT	CAA	TTA	AGA	GGA	CAA	ATT	CAA
Pro	Ala	Thr	Ala	Pro	Ser	Gln	CJA	Gly	Val	Asn	Ser	Pro	Val	Asn	Val>
	:	7:	30		7	740			750			76	50		
	•		•	•				*	*		•,		•	•	
ACA	ACT	ACA	GTT	GAT	GCT	TAA	ACA	TCA	CTT	GCT	AAA	ATT	GAA	TAA	GČT
TGT	TGA	TGT	CAA	CTA	CGA	TTA	TGT	AGT	GAA	CGA	TTT	TAA	CTT	TTA	CGA
1111	IHE	Inf	vai	ASP	WIG	ASI	1111	ser	ren	A19	Lys	He	Glu	Asn	Ales
770			780		•	79	90		1	800			810		٠
•		•	•		•		•	•		•		• 1	•		•
ATT					C 1 C	C B B	200	~~		FD-771 %	~~~				
97 2 2	AGA	ATG	ATA	AGT	GAT	CWV	WGG	GCA	AAT	TTA	GGT	GC1	TTC	CAA	AAT.
TAA	TCT	TAC	TAT	TCA	CTA	GTT	TCC	CGT	TTA	AAT	CCA	CGA	AAG	GTT	AAT TTA Asp>

820 830 840 850 860 AGA CTT GAA TCT ATA AAG AAT AGT ACT GAG TAT GCA ATT GAA AAT CTA TCT GAA CTT AGA TAT TTC TTA TCA TGA CTC ATA CGT TAA CTT TTA GAT Arg Leu Glu Ser Ile Lys Asn Ser Thr Glu Tyr Ala Ile Glu Asn Leu> 880 890 AAA GCA TCT TAT GCT CAA ATA AAA GAT GCT ACA ATG ACA GAT GAG GTT TTT CGT AGA ATA CGA GTT TAT TTT CTA CGA TGT TAC TGT CTA CTC CAA Lys Ala Ser Tyr Ala Gln Ile Lys Asp Ala Thr Met Thr Asp Glu Val> 920 930 940 . GTA GCA GCA ACA ACT AAT ATG ATT TTA ACA CAA TCT GCA ATG GCA ATG CAT CGT CGT TGT TGA TTA TAC TAA AAT TGT GTT AGA CGT TAC CGT TAC Val Ala Ala Thr Thr Asn Met Ile Leu Thr Gln Ser Ala Met Ala Met> 980 1000 ATT GCG CAG GCT AAT CAA GTT CCC CAA TAT GTT TTG TCA TTG CTT AGA TAA CGC GTC CGA TTA GTT CAA GGG GTT ATA CAA AAC AGT AAC GAA TCT Ile Ala Gln Ala Asn Gln Val Pro Gln Tyr Val Leu Ser Leu Leu Arg> 1010 TAA ATT

FIGURE 40 (3 of 3)

#### Alignment List

Search Anal Search from Date: Octob Time: 15:03	1 to er 2	0 10	ll w	uenc	e: B ori	31-4 gin :	1kD = 1		Sco	re R	egio	n fr	om 1	e ma to ore:	1011	-
Database: U	serFo	olde	r: 4	l kD	Flag	gell:	in c	lone	S							
) (1)		*	;	10	*		20		*	30	•	*		40	•	
B31-41kD	ATG TAC	TTA AAT	ATC TAG	AAT TTA	CAT GTA	AAT ATT	ACA TGT	TCA AGT	GCT CGA	ATT TAA	AAT ATT	GCT -CGA	TCA AGT	AGA	AAT TTA	TAA
1. KA-41k [ 3996 ]	D 	•••		10	• • •	• • •	20			30	•••	•••	• • •	40	• • •	>
2. P-Gau-	4	·		10			20	•••		30	•••	• • •	• • •	40		>
3. BO-41k	D 	• • •	:				20		• • •	30	• • •	•••		40		>
4. DK29-4	1		:	10		•••	20	• • •	• • •	30		• • •		40		>
5. PKO-411 [ 3672 ]	_	• • •		10	• • •		20	•••		30				40	• • •.	>
	50			60			•	70			80			90		
B31-41kD	cce ccc	TTA AAT	AAC TTG	GCT CGA	GCT CGA	* AAT TTA	CTT GAA	AGT TCA	* AAA TTT	ACT TGA	* CAD	GAA CTT	AAG TTC	العلم #	TCT AGA	AGT TCA
1. KA-41ki [ 3996 ]		• • .•		60			•	70	•		80		•••	90		>
2. P-Gau-	450 .c.		t	60				70		c	80	g	 4. • •	90		>
3. BO-41ki [ 3684 ]	D50			60				70			P0			00		>
4. DK29-4:	150	• • •		60			•	70			80			90		>
5. PKO-411		• • •	t	60	•••	•••	•	70			80			90 .c.		>
	10	00	*	:	110		•	120			13	30	-		L40	
B31-41kD	CCC	TAC ATG	AGA TCT	ATT AAT	AAT ATT	CGA GCT	GCT CGA	TCT	GAT	GAT CTA	TOO CGA	GCT CGA	GGC CCG	ATG TAC	* GGA CCT	GTT CAA

	1. KA-41kI 3996 ]															L40 •••	>
I	2. P-Gau-4 3696 ]	t	0			10			120		• • •		30	t	• • •	g	>
ſ	3. BO-41kI 3684 ]	) 10	0			10		•••	120		•••	1:	30			g	>
I	4. DK29-41 3672 }	t	00			10	a	•••		• • •				t		.40 g	
t	5. PKO-41k 3672 ]	t	0	•••			• • •		120	•••	• • •	1:	30		•••		>
		*	150			16	50 *	*	;	170		*	180			19	
B	31-41kD			AAG	ATT	AAT	GCT	CAA	ATA		GGT	TTG	TCA	CAA			
	1. KA-41kI 3996 ]																90
ĩ	2. P-Gau-4	• • • •	150 c		•••	16	50	•••	• • •	170 .c.	c	a	180				0
I	3. BO-41kI 3684 ]	•••	150 c	• • •			50		• • •	170	c	a	180	• • •	• • •	19	0 >
	4. DK29-41 3672 ]									170			180		•••		00
	5. PKO-41) 3672 ]														• • •	19	90 >
				200		*	210		*	2	20		2	230		•	240
B.	31-41kD	AAT ATT	ACT TGA	TCA AGT	AAG	GCT	ATT	AAT	TTT		CAG	ACA	ACA	GAA	GGG	AAT	TTA
I	1. KA-41kI 3996 ]	•••	•••	200	•••	•••	210	• • •	•••		20	• • •		230	•••		240 >
	2. P-Gau-6										20			230	a	• • •	240 >
. [	3. BO-41ki 3684 ]			200							20	• • •		230	.,a	•••	240
	4. DK29-4: 3672 ]									2:				230			240 g>
·I	5. PKO-413				a			• • •			20	• • •		230			240

				2	50	•	٠	260 *		•	270			2	80		
B	31-41kD	AAT ATT	GAA CTT	GTA CAT	GAA	AAA	GTC	TTA	GTA	AGA	ATG	AAG	GAA	JATA	CCA	بتعتب	CAA
I	1. KA-41k 3996 ]	Ð	•••		50			260		•••	270			2	80		;
	2. P-Gau- 3696 ]																
	3. BO-41k	D		2.	50		:	260			270			2	90	-	
	3684 ]	•••	• • •	• • •	•••`	`•••	t	• • •	• • •	• • •	•••	a	•••	a	•••	• • •	>
I	4. DK29-4 3672 ]	1	•••	2:	50		t	260	•••	•••	270	.∵a	·	2: a	B0 	• • •	>
I	5. PKO-41 3672 ]	k	·	2:	50	•••	t	260	•••	•••	270 	a	• • •	2: a	30		>
	:	290		* ,	300			3:	10	*		320		*	330		*
B	31-41kD	TCA AGT	GGT	AAC	GGC	ACA	TAT	TCA	GAT	GCA	GAC	ACA	CCT	للحكك	2002	C11	
I	1. KA-41k 3996 ]	290		• • •	300			3:	10	••,•		320			330		>
I	2. P-Gau-3	290		,	300			٦.	10		-	220					
	3. BO-41ki 3684 ]	290			300			٦.	10		-	200					
	4. DK29-4	290			300			21	10	-		200		,	~ ~ ~		
٠	3672 ] 5. PKO-412															• • •	>
Ţ	3672 ]	•••	•••	•••	a	g	•••	•••		t	•••	•••	· · ·	·	330	g	>
•		34	*	*	3	*					•		_			_	
·B3	31-41kD	GAA CTT	ATA TAT	GAG CTC	CAA GTT	CTT GAA	ACA TGT	GAC CTG	GAA	للملاك	ጉልጥ	ACA.	ענאבו ע	~~	~~~	ĆAA GIT	GCT CGA
Į	1. KA-41ki 3996 }	34		• • •		50	• • •	• • •	360	•••		37	0			80	>
	2. P-Gau-4	1 34	0		3	50			360			27	n		_		
	3. BO-41ki 3684 J	3'4	0		3	50			360			27	ń				•
	4. DK29-4;										- • •	•	0	• • •		80 80	>

I	3672 ]	• • •	•••	• • •	• • •		• • •,	•••		•••		•••	•••		• • •	• • •	>
Į	5. PKO-411 3672 ]	k 3	40	• • •	•••	350		• • •	360		•••						>
В	31-41kD	* CAA GTT	390 TAT ATA	AAC	caa Gm	ATG	CAC	ATG	TTA	410 TCA AGT	AAC	AAA	420 TCT AGA	GCT	TCT	4 CAA GTT	
1	1. KA-41kI 3996 _r )	)	390			41	00		•	410		•	420	•		. 4	30
I	2. P-Gau-4		390		• • •	40	00		g	410	:	٠.٠	420		c	4:	30
I	3. BO-41kI 3684 ]			• • •		4(	00	• • •	g	410	•••	• • •	420	•••	,c	4:	30
I	4. DK29-41 3672 ]	L	390		• • •	4(	00	• • •	g	410	• • •		420		c	4:	30
Į	5. PKO-41k 3672 ]	•••	390	• • •	;·••	4(	00	• • •	g	410	• • •	•••	420	• • •		43	30
В:	31-41kD	* GTA CAT	AGA°	ACA TGT	GCT	GAA	GAG	CTT GAA	GGA	ATG	CAG	CCT	GCA	444		AAC TTG	202
I	1. KA-41kD 3996 ]			140	•••	• • •	450		• • •	46	• • •	• • • alg•.		170		• • •	480
ı	2. P-Gau-4 3696 ]	•••	.a.	140	• • •	•	450 	•		46	50			170			480 >
I	3. BO-41kD 3684 ]	• • • •	.a.	140		• • •	450 			46	50	•••		170	• • •	•••	480 •••>
I	4. DK29-41 3672 ]	•••		40	• • •	• • •	450 a	•••		46	50 a	• • •		170	c		480 >
ſ	5. PKO-41k 3672 ]		.a.			•••	450 •••		•••	46	50	• • •		170	• • •	• • •	480 >
			*		0	*		600 *	•	*	510			52	*	*	
B.	31-41kD	CCA GGT	GCA CGT	TCA AGT	CTT GAA	TCA AGT	CCC	CTT GAA	CAA GTT	GCG CGC	TCT AGA	TGG ACC	ACT TGA	ATT TAA	AGA TCT	GTT CAA	CAT GTA
Į	1. KA-41kD 3996 )	• • • •	•••	49	0	• • •		500 tc.		•••	510		•••	52	0	• • •	>
Į	2. P-Gau-4 3696 ]			49	0		a	500 tc.		t	510	• • •		52	0		>

1	3. BO-411 [ 3684 ]	Φ 	• • •	4	90	•••	a	500 tc.	• • •	t	510		•••	5	20	• • • •	>
I	4. DK29-4		9		90	• • •	a	500 tc.	•••	t	510	•••	• • •	5	20	• • • •	>
I	5. PKO-41 3672 ]		• • •	4	90	•••	a	500 tc.	• • •	t	510	•••	•••	5	20	• • •	>
		530		*	540	, *	•	5	50	*		560		*	570 *	)	•
B	31-41kD	GTT	GGA	GCA	ACC	CAA	GAT	GAA	CCT	Aur	GCT CGA	GTA CAT	<b>አ</b> አ ካ ጥ	بلغاية لا ر	(T) N (T)		GCT
I	1. KA-41k 3996 ]	530			540		•	5	50			 560			E30		
	2. P-Gau- 3696 ]	530			540			5	50		,	560					
	3. BO-41k 3684 ]	530			540			51	50			: <b>c</b> n					
	4. DK29-4	530			540			5	50								
	3672 ] 5. PKO-41	530			540			. 50	50								
•	3672 ]	9	•••	•••	.at	•••.	•••	• • •	a	• • •	• • •	•••	•••	• • ,•	• • •	t	>
		51	30 *	*	:	590		•	600		_	61	١٥		. (	520	
	31-41kD	51 AAT	30 * GTT	* GCA	; TAA	590 •	ידיר	# #	600 *	CAC	*	61	0	*	. (	520	
B3	31-41kD 1. KA-41k	51 TAA TTA	GTT CAA	GCA CGT	TAA ATT	SPO CTT GAA	TTÇ AAG	* TCT AGA	GGT CCA	GAG CTC	* GGA CCT	61 GCT CGA	CAA GTT	* ACT TGA	GCT CGA	520 CAG GTC	GCT CGA
B3	31-41kD 1. KA-41k 3996 ] 2. P-Gau-	58 AAT TTA D 58	GTT CAA	GCA CGT	TAA TTA	CTT GAA	TTC AAG	* TCT AGA	600 * GGT CCA 600	GAG CTC	GGA CCT	GCT CGA 61	CAA GTT	ACT TGA	GCT CGA	CAG GTC	GCT CGA
BE	31-41kD 1. KA-41k 3996 ]	58 AAT TTA D 58	GTT CAA	GCA CGT	AAT TTA	590 CTT GAA 590 	TTÇ AAG 	TCT AGA	600 * GGT CCA 600 	GAG CTC	GGA CCT	61 GCT CGA 61  61	CAA GTT 0	ACT TGA	GCT CGA	CAG GTC 520 	GCT CGA >
B3	31-41kD 1. KA-41k 3996 ] 2. P-Gau- 3696 ] 3. BO-41k	58 AAT TTA D 58	GTT CAA	GCA CGT	ATTA	590 CTT GAA 590  590	TTC AAG	* TCT AGA	600 *GGT CCA 600  600	GAG CTC	GGA CCT	61 GCT CGA 61  61	CAA GTT 0	ACT TGA  g	GCT CGA	CAG GTC 520 520	GCT CGA >
B3	1. KA-41k 3996 ] 2. P-Gau- 3696 ] 3. BO-41k 3684 ] 4. DK29-4 3672 ]	58 AAT TTA D 58  4 58  D 58	GTT CAA 30 30 30	GCA CGT	TTA	590 CTT GAA 590  590 	TTC AAG	* TCT AGA	600 * GGT CCA 600  600 	GAG CTC	GGA CCT	61 CGA 61  61 	CAA GTT 0 0	* ACT TGA g	GCT CGA	520 CAG GTC 520  520	GCT CGA >
B3	1. KA-41k 3996 ] 2. P-Gau- 3696 ] 3. BO-41k 3684 ] 4. DK29-4	58 AAT TTA D 58  4 58  D 58	GTT CAA 30 30 30	GCA CGT	TTA	590 CTT GAA 590  590 	TTC AAG	* TCT AGA	600 * GGT CCA 600  600 	GAG CTC	GGA CCT	61 CGA 61  61 	CAA GTT 0 0	* ACT TGA g	GCT CGA	520 CAG GTC 520  520	GCT CGA >
B3	1. KA-41k 3996 ] 2. P-Gau- 3696 ] 3. BO-41k 3684 ] 4. DK29-4 3672 ] 5. PKO-411	58 AAT TTA D 58  D 58 	GTT CAA 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 3	GCA CGT	AAT TTA	590 CTT GAA 590  590  690	TTC AAG	TCT AGA	600 GGT CCA 600  600 	GAG CTC	GGA CCT	61 CGA 61  61  61	CAA GTT 0  0	# ACT TGA g	GCT CGA	520 CAG GTC 520  520  520	GCT CGA >
B3	1. KA-41k 3996 ] 2. P-Gau- 3696 ] 3. BO-41k 3684 ] 4. DK29-4 3672 ]	58 AAT TTA D 58  D 58  C 58	GTT CAA  30 30 30 40 50 630	GCA CGT	AAT TTA	590 CTT GAA 590  590  690  64	TTC AAG	* TCT AGA g	600 GGT CCA 600  600 	GAG CTC	GGA	61 61 61	CAA GTT 0  0  0	# ACT TGA g g	GCT CGA	520 CAG GTC 520  520  520 	GCT CGA >

1. KA-41kD [ 3996 ]	• • • • • • • • • • • • • • • • • • • •	• • • • • •	• • • • • • • • • • • • • • • • • • • •	660	•• ••• •••>
2. P-Gau-4 [ 3696 ]	630 t	640 	650 g.a	660 g .	670 .a a>
3. BO-41kD		640	650		
4. DK29-41	•	640	650		
5. PKO-41k [ 3672 ]	630	640	CED		
*	680	690	<u> </u>	710	720
		n AGA GII C	CG CCT CAA	AAT TCT CCT GT ITA AGA GGA CA	
1. KA-41kD [ 3996 ]	680	690	700	710	720
2. P-Gau-4 [ 3696 ]	680	690 . a	700 .t		• •
3. BO-41kD [ 3684 ]		690	700	<b></b> -	720
4. DK29-41		690	. 300		720
5. PKO-41k [ 3672 ]	680	600	200		•
:	730	740	750	-	
B31-41kD ACA	ACT ACA GTT GAT TGA TGT CAA CTA	* ርጥ አአጥ አር	* *	760 T AAA ATT GAA	AAT GCT
	730	740		760	TTA CGA
2. P-Gau-4 [ 3696 ]	730	740	750	760	•••
3. BO-41kD	730	740	750	760	>
4. DK29-41	c 730	740	· · · · · · · · · · · · · · · · · · ·	760	>
5. PKO-41k	730	740	750	· · · · a	>
[ 3672 ]	c	•••		760 ·a	>

	770	780		790		300	. 81	0
B31-41kD	ATT AGA TAA TCT	ATG ATA	AGT GAT	CAA AGG	GCA AAT	TTA GGT	GCT TT	C CAA AAT G GTT TTA
1. KA-41 [ 3996 ]			•••	790		300	81	-
2. P-Gau [ 3696 ]	-770 	780		790 a		800	81	0
3. BO-41 [ 3684 ]	k770	780	•••	790 a		800	81	
4. DK29- [ 3672 ]		780 		790 a		800	81	0>
5. PKO-4 [ 3672 ]	1770	780 		790 a			81	0
	820		830	. 840	•	850	*	860
B31-41kD								A AAT CTA T TTA GAT
1. KA-41 [ 3996 ]				840		850		860
2. P-Gau [ 3696 ]								860
3. BO-41 [ 3684 ]						850 t		860
	41 820			840 g				860 c>
5. PKO-4	1k 820		830	840	· · · · · · · · · · · · · · · · · · ·	850 t	•••	860
•	87 <u>(</u>	0	880	*	890	900	,	910
B31-41kD	AAA GC	A TCT TAT T AGA AT	r GCT CAM A CGA GT	AAA ATA A	A GAT GCI CTA CGA	ACA ATG TGT TAC	ACA GA	T GAG GTT 'A CTC CAA
1. KA-4: [ 3996 ]	1kD 87	o • • • • • • • • • • • • • • • • • • •	880	• • • • • • •	890	900	•••	910
2. P-Gan [ 3696 ]	u-4 87	0	880	• • • • • • •	890	900	•••	910
3. BO-4 [ 3684 ]	1kD 87							910
	-41 87							910

5. PKO-4.	1k	870	)		8	380			890			900	)		_	110
[ 3672 ]	• • •	• • •	• • •	• • •	• • • •	• • • •	• • • •					• • •	••	• • • •		10
																•••-
	•		920		• .	930	•	•		940			950	•		960
B31-41kD	GTA. CAT	GCA CGT	GCA CGI	ACA TG1	ACT	TAA T	TAC	TAA	TTI AA:	A ACA	CAA	TCI	. cci	ATC	* GCA CGT	ATG TAC
1. KA-411 [ 3996 ]	Ð		920	••		930				240						
2. P-Gau-	4		920			030								•		960 ···>
3. BO-41k	. Œ	•	920			930				40						
[ 3684 ]	• • •	• • •	t	• • •	• • •	• • •	.gt	• • •	• • •	t	• • •	•••	•••	• • •		900
4. DK29-4 [ 3672 ]	1	•	920			030			_							
5. PKO-41	k		920								•••			•••	•••	•••>
[ 3672 ]	•••	•••	t	• • •		a	.gt	•••		40 t	• • •	•••	950 •••	• • •	· • • •	960 >
es.				70 *	•		980		•	990						
B31-41kD	ATT (	GCG CGC	CAG GTC	GCT CGA	TAA ATT	CAA GTT	GTT CAA	~~~	~			TTG AAC	TCA AGT	TTG	CTT .	AGA
1. KA-41ki [ 3996 ]	•••		97	0		g	80			990			100		CAA	
2 2 2 2 2						,	•••	• • •	• • •	•••	• • •	•••	• • •	• • •	• • •	• • • •
2. P-Gau-4	••••	a	97	0	• • •	9	80	t	•••	990	• • •	• • •	100	0		
3. BO-41kI [ 3684 ]	)		97	O		٥	80	•		990		•	100	n		
4. DK29-41			97	0		q	80			000					•••	· · ·>
[ 3672 ]	••••	• •	a	• • •		• • •	• • •	t	• • •	330	• • • •	• • •			• • • •	>
5. PKO-41k [ 3672 ]			97	n		9.		t		990			100			
							Ť	•	- <b></b>	7	•••	•••	• •	• • •	• • • •	>
10	10										•					
	TAA ATT			•												
2. P-Gaul0 [ 3696 ]	10		•													

Sequence Ran	ge: 1	to 82	2				•								
			10	_		20			30			4	0		
OspA-B31	ATG AATTAC TI	AA AAA TTT TTT	TAT .	TTA .	TTG AAC	GGA CCT	ATA TAT	GGT CCA	CTA	ATA TAT	ATT AAT	CCC .	TTA AAT	ATA TAT	CCT CCT
OspA-B31 [ 3288 ]		· · · · ·	10		•••	20 	•••	•••	30	٠	•••	4	0	•••	>
OspA-KA [ 3288 ]	••• •		10		•••	20	• • •	•••	30	• • •		4	0	• • •	···>
OSPA-N40 [ 3276 ]	• • • • •		10	•••	•••	20	•••		30	•••	•••	4	0	• • •	>
OspA-ZS7 [ 3264 ]			10	•••		20		•••	30			4	0	•••	>
OspA-25015 { 2802 ]	••••		10			20	. • • •		30	• • •	• • •	t	0		>
OSPA-TRO [ 2648 ]			10		•••	20	•••	•••		•••	•••		0		>
OspA-K48 [ 2584 ]		•• ••	10		•••	20	•••	•••	30	•••		4	0		>
Ospa-HE 11 [ 2580 ]		•	10			20	•••	•••	30	• • •	• • •	4	0	•••	>
Ospa-DK29 [ 2566 ]		•• ••	10		• • •	20	• • •	•••	30		•••		0		>
OspA-Ip90 [ 2562 ]	••••					20			30		• • •	a	0		>
OspA-B0 [ 2558 ]			10	•••	•••	20		•••	30	• • •	• • •,		o • • • •	::-	>
OSPA-IP3 [ 2558 ]	••••		10	•••	•••	20			30	• • •			0	• • •	>
OspA-PKO [ 2558 ]	••••	• • • •	10	• • •		20	• • •	• • •	30	• • •	•••	• • •		• • •	>
Ospa-acai [ 2556 ]					•••	20	•••	• • •	30		• • •		• • • •	•••	>
ospa-P-GAU [ 2544 ]	•••			•••	•••	20	• • • •		30	•••	• • •	• • •		•••	>
	50	*	60		*		70	•		80		•	90		<b>t</b>
OspA-B31	TGT ACA	AAG CA	TAA AJ ATT T	GTT CAÀ	AGC	AGC	CTI GAA	CIC	GAG CTC	AAA TTT	AAC	AGC TCG	GTT CAA	TCA AGT	CAT

FIGURE 42 (1 of 16)

	/
111/	133
• • • •	

OspA-B31 [ 3288 ]	50	60	70	80	90
Ospa-Ka [ 3288 ]	50:	60	70	80	90
Ospa-N40 [ 3276 ]	50	60	70	80	90
OspA-ZS7 [ 3264 ]	50	60	70	80	90>
OspA-25015 [ 2802 ]	50	60	70	80	90
OspA-TRO [ 2648 ]	50	60	70 t	80	90
OspA-K48 [ 2584 ].	50	60	70t	80at	90
OSPA-HE 11 [ 2580 ]	50	60	70	80 at	90
OspA-DK29 [ 2566 ]	50	60	70 t	80 at	90
OspA-Ip90 [ 2562 ]	50	60	70 t	80 at	90
0spA-B0 [ 2558 ]	50	60	70 t	80	90 .c>
OSPA-IP3 [ 2558 ]	50 c	60	70 t	80 a	90 .c>
Ospa-PKO [ 2558 ]	50 c	60	70 t	80 a	90 .c>
Ospa-ACAI [ 2556 ]	50	60	70 t	80 a	90 .c>
ospA-P-GAU [ 2544 ]	50 c	60	70 t	80 a	90 .c>
•	100	110	120	130	140
OspA-B31	GAT TTG CCT CTA AAC GGA	GGT GAA ATC	AAA GTT CTT TTT CAA GAA	GTA AGC AAA GAA CAT TCG TTT CTT	AAA AAC AAA TTT TTG TTT
OspA-B31 [ 3288 ]	100	110	120	130	140>
Ospa-Ka [ 3288 ]	100	110	120	130	140>
OspA-N40	100	110	120	130	140

FIGURE 42 (2 of 16)

### SUBSTITUTE SHEET (RULE 26)

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[ 3276 ]		c		···· ··· ··· >
OspA-ZS7 [ 3264 ]	100 110	120 c		140>
OspA-25015 [ 2802 ]	100 110	120	130	
OspA-TRO [ 2648 ]	100 110	120	130	140 g>
OspA-K48 [ 2584 ]	100 110	c. 120		140 g>
OspA-HE 11 [ 2580 ]	100 110	120	<del>-1</del> 30 t	140 g>
OspA-DK29 [ 2566 ]	100 110	120 c	130 t	140 g>
OspA-Ip90 [ 2562 ]	100 110	120 c	130 t	140 g>
OspA-BO [ 2558 ]	100 110g	120	130 t	140 g>
OSPA-IP3 [ 2558 ]	100 110g	120 t	130	140 g>
OspA-PKO [ 2558 ]	100 110g	120	130 t	140 g>
OspA-ACAI [ 2556 ]	100 110g	120 '	130 t	140 g>
ospa-P-Gau [ 2544 ]	. 100 110	120	130 t	140 g>
	150 160	170	180	190
OspA-B31	GAC GGC AAG TAC GAT CT CTG CCG TTC ATG CTA GA	TA ATT GCA ACA GTÁ AT TAA CGT TGT CAT	GAC AAG CTT CTG TTC GAA	GAG CTT AAA CTC GAA TTT
OspA-B31 [ 3288 ]	150 160	170	180	190
Ospa-Ka [ 3288 ]	150 160	170	180	190
OspA-N40 [ 3276 ]	150 160	170	180	190
OspA-ZS7 [ 3264 ]	150 160	170	180	190
OspA-25015 [ 2802 ]	150 160	170	180	190

FIGURE 42 (3 of 16)

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Ospa-TRO [ 2648 ]	t	150 :t				160	• ••	g	170	• ••		18	0	a		190
OspA-K48 [ 2584 ]	• • •	150		a		160		g	170	• • •		18	0			190
OspA-HE 11 [ 2580 ]	t	150 :t		a			9				• • •	18 a	0		: • ••	190
OspA-DK29 [ 2566 ]		150 t							170			18	0			190
OspA-Ip90 [ 2562 ]	t	150		٠					170		• • • •	180				190
OspA-BO [ 2558 ]	•••	150 t				160	.ag		170	• • •		180	) . a	• • • •		190 a>
OSPA-IP3 [ 2558 ]		150 t			ag.	60	. ag		170		•••	180	). a	• • • •		i90
Ospa-PKO - 1 [ 2558 ]		150			1	.60			170			180	1	•	-	L90
Ospa-acai [ 2556 ]		150			1	.60			170			180			,	.90
ospA-P-GAU [ 2544 ]	•••	150 t	•••				.ag		170		•••	180	a		1 a	90.
		2	00			210				20	_	:	230			240
OspA-B31	GGA CCT	ACT TGA	TCT AGA	GAT CTA	AAA TTT	AAC TTG	AAT ATT	GGA CCT	υ⁄-r	CCZ	GTA CAT	CTT GAA	GAA CTT	GGC CCG	GTA CAT	AAA TTT
OspA-B31 [ 3288 ]		2	00	• • •	• • •	210	•••				•••	·	230	• • •	• • •	240
OspA-KA [ 3288 ]	•••	2	00	•••		210	• • •		22	0	• • •	2			• • •	240
OspA-N40 [ 3276 ]	•••	2	00		• • •	210	•••	•••		0			30	• • •	• • •	240
Ospa-ZS7 [ 3264 ]	•••	2	00	•••	•••	210	•••						30	•••	'	240
OspA-25015 [ 2802 ]	•••	a	00			210		• • •			g	2	30	• • •		240
OspA-TRO [ 2648 ]	•••		00	• • •		210 .g.	c	t	22		ac.	2	30	t	.a.	240
OspA-K48 [ 2584 ]	•••		00			210	c	t	22		ac.	2.	30	t	.a.	240

FIGURE 42 (4 of 16)

OSPA-HE 11 [ 2580 ]	200		210 c	t	220 ac.	230	t .a.	240 >
OspA-DK29 [ 2566 ]	200	• • • • • •	210 c	t .	220 ac.	230		240 >
OspA-Ip90 [ 2562 ]	200	•••	210 c	t .	220 ac.	230		
OspA-BO [ 2558 ]	200		210 g	t	220 gs	230		240 >
OSPA-IP3 [ 2558 ]	200	•••	210 g	t .	9	230		240
OspA-PKO [ 2558 ]	200		210 g	.,.t .	gg	230		240 >
Ospa-ACAI [ 2556 ]	200		210 g	t .	9	230		240 >
ospa-P-GAU [ 2544 ]	200		210 g	t .	9	230		240 >
	2.	50	260	_	270	28	30	
OspA-B31	GCT GAC AAA	AGT AAA	GTA AAA	A ATT	CA ATT TCT	GAC GAT	CTA GGT GAT CCA	CAA GTT
	CGA CTG TIT	104 111	Un. 111					
OspA-B31 [ 3288 ]	2	50	260		270	28	•	>
	2	50		••••		•	30 •••••••	>
[ 3288 ] Ospa-Ka	2	50	260	••••	270	28 28 28	30 •••••••	>
[ 3288 ] OspA-KA [ 3288 ] OspA-N40	2 2 2	50  50	260 260 260	••••	270 270 270 270	28 28	30 30 30 30	>
[ 3288 ] OspA-KA [ 3288 ] OspA-N40 [ 3276 ] OspA-Z57	2 2 2 2	50 50 50	260 260 260	••••	270 270 270 270	28 28 28	30 30 30 30	>
[ 3288 ] OSPA-KA [ 3288 ] OSPA-N40 [ 3276 ] OSPA-ZS7 [ 3264 ] OSPA-25015	2 2 2 2	50 	260 		270 270 270 270 270 270 270	28	30 	>> ac.>
[ 3288 ] OSPA-KA [ 3288 ] OSPA-N40 [ 3276 ] OSPA-Z57 [ 3264 ] OSPA-25015 [ 2802 ] OSPA-TRO	2 2 2 2	50 	260 		270270270270270270270	28 28 21	30 30 30 30 30 30 30 30 30 30 30	>> ac.>
[ 3288 ] OSPA-KA [ 3288 ] OSPA-N40 [ 3276 ] OSPA-ZS7 [ 3264 ] OSPA-Z5015 [ 2802 ] OSPA-TRO [ 2648 ] OSPA-K48	2 2 2 2	50 50 50 50 50 50	260 		270270270270270270270270270270	28 28 28 29 29 21	30 30 30 30 30 30 30 30 30 30 30 30 30 3	>> ac.>
[ 3288 ] OSPA-KA [ 3288 ] OSPA-N40 [ 3276 ] OSPA-ZS7 [ 3264 ] OSPA-Z5015 [ 2802 ] OSPA-TRO [ 2648 ] OSPA-K48 [ 2584 ] OSPA-HE 11	2 2 2 2	50 50 50 50 50 50	260 		270 270 270 270 270 270 270 270 270 270 270 270 270 270 270	28 28 21	30 30 30 30 30 30 30 30 30 30 30 30 30 3	>> ac.> a>

FIGURE 42 (5 of 16)

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	[ 2562 ]	a	•••	• •		• • • •	.c.	• • • •	• • • •		•••	g.,	9		• • •	a	a>
	OspA-BO [ 2558 ]	.a.	٠		250			260			270 		•••		80	٠.,	a>
	OSPA-IP3 [ 2558 ]	.a.	•••		50	• • •		260			270		•••		80	a.,	a>
	Ospa-PKO [ 2558 ]	.a.	•••		50	•••		260		•••	270		•••	2	80	•••	a>
	OSDA-ACAI [ 2556 ]	.a.	•••		50	• • •	.c.	260		•••	270	g.,	• • •	2	во	a	a'>
	ospa-P-GAU [ 2544 ]				50			260	•••		270.		• • •	2	80	a	a>
		290			300			3:	10		3	320			330		
	OspA-B31	ACC TGG	ACA TOT	CTT GAA	GAA CTT	GTT CAA	TTC AAG	AAA TTT	GAA CTT	GAT	66C 6CC	AAA TTT	ACA TGT	* CTA GAT	GTA CAT	TCA AGT	AAA TTT
	OspA-B31 [ 3288 ]	290		• • •	300		• • •	33				20		• • •	330	• • •	>
	Ospa-Ka [ 3288 ]	290	• • •		300			31	LO		3	20			330	•••	•
	Ospa-N40 [ 3276 ]	290			300							20	• • •		330		>
	Ospa-ZS7 [ 3264 ]	290						, 31		•••		20			330	•••	>
	OspA-25015 [ 2802 ]				300		a	31	0			20		t	330	•••	>
	Ospa-TRO [ 2648 ]	290			300			31	0		3:	20			330		
	OspA-K48 [ 2584 ]	290 t			300	a		31	0	• • •	.c.	20			330		
1	Ospa-HE 11 [ 2580 ]	290		t	300	a.c	•••	31	0	•••	3:	20	1	t :	330	g	>
1	Ospa-DK29 [ 2566 ]					a	•••	31	0	• • • •	32	20	1	3 <b>t</b> ,	330	• • •	>
	OspA-Ip90 [ 2562 ]	290	• • •	t	300	a.c	•••	31	0	•••	32		1		330		>
	OspA-BO [ 2558 ]	290	• • •	t.c	300	c	• • •	31		•••	32	20		3	330	` .	.g.>
	OSPA-IP3 [ 2558 ]	290			300	·		310	0		. 32	20		-	เรก		
															_		-

FIGURE 42 (6 of 16)

OspA-PKO [ 2558 ]	290 t.c	300	310	320 t	330gg.>
Ospa-ACAI [ 2556 ]	290 t.c	300 c	310	320 t	
ospa-P-GAU [ 2544 ]	290 t.c		310	320 t	330 gg.>
	340	350	360	· 370	380
OspA-B31	AAA GTA ACT TTT CAT TGA	TCC AAA GAC AGG TTT CTG	AAG TCA TCA TTC AGT AGT	ACA GAA GAA AAA TGT-CTT-CTT-TTT	TTC AAT GAA AAG TTA CTT
OspA-B31 [ 3288 ]	340	350	360	370	380>
Ospa-Ka [ 3288 ]	340	350		370	
OspA-N40 [ 3276 ]	340		360	370	
OspA-ZS7 [ 3264 ]	340	350	360	370	380
OspA-25015 [ 2802 ]	340	350	360		380
OspA-TRO [ 2648 ]	340	350	360	,	380
OspA-K48 [ 2584 ]	340	350	360	370	380
OspA-HE 11 [ 2580 ]	340	350	360	370	380
Ospa-DK29 [ 2566 ]	340	350	360	370	
OspA-Ip90 [ 2562 ]	. 340	350	360	370	380
OspA-BO [ 2558 ]	340	350	360		380
OSPA-IP3 [ 2558 ]	340	350	360	370	380
OspA-PKO [ 2558 ]	340	350	360	370	380
Ospa-ACAI [ 2556 ]	340	350	360	370tg	380 .

FIGURE 42 (7 of 16)

ospa-P-GAU [ 2544 ]	340	.gt	350 .g	a a	360 a	t	70tg	>
	390	•	400	•	410	•	420	430
OspA-B31	AAA GGT TTT CCA	GAA GTA CTT CAT	AGA CTT	TTT T	AT TAT 1	ICT TCT	GCA GAC	GGA ACC AGA CCT TGG TCT
OspA-B31 [ 3288 ],		• • • • • • • • • • • • • • • • • • • •	• • • • • •	• • • •		• • • • •		430>
OspA-KĀ [ 3288 ]		•••		••••	410	•••••	420	430
OspA-N40 [ 3276 ]	390	•••	400		410		420	430
OspA-ZS7 . [ 3264 ]	390		400		410		420	430
OspA-25015 [ 2802 ]	390 c	t	400 gt		410 g.g	· · · · · ·	420 a	430 t.>
OspA-TRO [ 2648 ]	390	t	400		410 c c	t	420 a	430 g>
OspA-K48 [ 2584 ]	390 g	ac.	400		410 g	t	420 a.t	430
OspA-HE 11 [ 2580 ]	390 g	a	400		410	t	420 a.t .	430
OspA-DK29 [ 2566 ]	390 g	ac.	400	c	410 gt	t	120 a.t .	430
OspA-Ip90 [ 2562 ]	390 g	c.	400	c	410 gt	t	120 a.t .	430
OspA-BO [ 2558 ]	390	t.g	400	c	410 c.g		120 a.a.t.	430
OSPA-IP3 [ 2558 ]	390	t.g	400	c	410 Cg		20 a.a.t.	430 a.>
OspA-PKO [ 2558 ]	390	t.g	400	<i>.</i> c	410 cg		20 a.a.t .	430 a.>
Ospa-ACAI [ 2556 ]	390	t.g	400 c.		410 cg		20 a. a.t .	430 a.>
ospA-P-GAU [ 2544 ]	390	t.g	400	c	410 cg		20 a.a.t.	430 a.>
	4	40	450		460	_	470	480
OspA-B31	CTT GAA		GGA ATT A	JAA AG	C GAT GG	A TCT G	GA AAA G	CT AAA GAG

FIGURE 42 (8 of 16)

	GAA	CTT	ATG	1CI	ccr	TAA	TTT	TCG	CTA	CCT	AGA	CCI	TIT	CGA	TTT	CTC
OspA-B31 [ 3288 ]	• • •	• • •	440	•••		450		•••	4	60	•••		470 	•••	• • •	480 >
OspA-KA [ 3288 ]	•••		440		•••	450	•••			60	• • •		470	• • •	·	480
Ospa-N40 [ 3276 ]			440	•••	.a.	450 •••	•••			60	•••	• • •	470 		• • •	480
OspA-ZS7 [ 3264 ]	•••		140	•••	.a.	450 •••	• • •		40	50	•••	• • •	470	•••	• • •	480
OspA-25015 [ 2802 ]	• • •		140	•••	•••	450 •••		•••		50	c		470	•••	• • •	480 a>
OspA-TRO [ 2648 ]			140	•••	.a.	450 a	•••				a.c		470			480 a>
OspA-K48 [ 2584 ]	•••		40	• • •	.ac	450 a	•••			50	c		470		• • •	480 a>
OspA-HE 11 [ 2580 ]			140		.ac	450 a	•••			0 aa.		•	470		• • •	480 a>
OspA-DK29 [ 2566 ]	• • •		140		.ac	450 a			46		<u>.</u> c		470			480 حة
OspA-Ip90 [ 2562 ]			140	•••	.ac	450 a	•••	•••		aa.	a.c		470	•••	• • •	480 a>
OspA-B0 [ 2558 ]	•••		140 t		.a.	450 • • g			46		a.c		170		• • •	480 a>
OSPA-IP3 [ 2558 ]	•••		140 t		.a.	450 ••g	•••		46		a.c		170	• • •	<b></b>	480 دع
OspA-PKO [ 2558 ]			t	•••		450 ••9			46		a.c		170	•••	• • •	480 a>
Ospa-ACAI [ 2556 ]	•••		40 t	•••	.a.	450 ••g	• • •	•••	46		a.c		170	•••		480 حة
ospA-P-GAU [ 2544 ]			t		.a.	450 ••9			46				70			480 a>
		_	49	0	_	5	500			510			52	0		
OspA-B31	GTT CAA	TTA AAT	AAA TTT	ccc ccc	TAT ATA	GTT CAA	CTT GAA	GAA CTT	GGA CCT	act Tga	CTA GAT	ACT TGA	GCT CGA	GAA . CTT '	AAA TTT	ACA TGT
OspA-B31 [ 3288 ]		•••	49	0	•••					510			52	0		>
OspA-KA [ 3288 ]	• •.•		49	0			500			510	•••		52	0		>

FIGURE 42 (9 of 16)

Ospa-N40 [ 3276 ]	490	500	510	520
OspA-ZS7 [ 3264 ]	490 a	500	510	520
OspA-2501 [ 2802 ]	490 acaa	500	510	520
OspA-TRO [ 2648 ]		500	510 • • • • • • • • • • • • • • • • • • •	520 cc>
OspA-K48 [ 2584 ]		500	510 • • • • • • • • • • • • • • • • • • •	cgg     520  530 
OspA-HE 11 [ 2580 ]	490at. ac.		510 g	5201 530
Ospa-DK29 [ 2566 ]	490 5		510 g	cgg 1 5201 530
OspA-Ip90 [ 2562 ]	490 5		510 g	cgg ! 520! 530
OspA-B0 [ 2558 ]	490 5	00	510 .aa g g aa	520 at gt.>
OSPA-IP3 [ 2558 ]	490 5	00	510 .aa g g aa	520
OspA-PKO [ 2558 ]	490 50	00	510 .aa g g aa	520
OSDA-ACAI [ 2556 ]	490 50	00	510 .aa g g aa	520t gt.>
ospA-P-GAU [ 2544 ]	490 50	00	510 .aa g g aa	520 t gt.>
	530 540	550	560	570
OspA-B31	ACA TTG GTG GTT AAA GAA G TGT AAC CAC CAA TTT CTT C	GA ACT GTT	ACT TTA AGC AA	A AAT ATT TCA
OspA-B31 [ 3288 ]	530 540	550	560	570
Ospa-ka	530 540	550	560	570
		•		

FIGURE 42 (10 of 16)

[ 3288 ]	• • • • • • • • • • • • • • • • • • • •	•••		• • • • • • • • • • • • • • • • • • • •	
Ospa-N40 [ 3276 ]	530		550		570 · · · · · · · · · · · · · · · · · · ·
OspA-ZS7 [ 3264 ]	530		550	560	570>
OspA-25015 [ 2802 ]	530	540	550	560 t.	
Ospa-TRO [ 2648 ]	530 aaa	540c		560 gt	
OspA-K48 [ 2584 ]	540 aaa			560- 5	70 .gct.>
OspA-HE 11 [ 2580 ]	540 aaa	c	550 .gc	560 5	70 .gc>
OspA-DK29 [ 2566 ]	540 aaa		550 c	560 5	70 .gct.>
OspA-Ip90 [ 2562 ]	540 a aaa	c	550 	560 S	70 c.c>
OspA-B0 [ 2558 ]	530aa	540	c	- 560	570 .g g.a g>
OSPA-IP3 [ 2558 ]	530aa	540	550	560	570 .g g.a g>
OspA-PKO [ 2558 ]	530aa	540	c	560	570 .g g.a g>
Ospa-ACAI [ 2556 ]	530 aa		550 c	560 t .	
ospA-P-GAU [ 2544 ]	530aa	540 a	550 c	560 t.	570 .g g.a g>
	580	<b>5</b> 90	600	610	620
OspA-B31			CA GTT GAA	CTT AAT GAC ACT G GAA TTA CTG TGA C	
OspA-B31 [ 3288 ]	580	590	600	610	620
OspA-KA [ 3288 ]	580	590	600	610	620
OspA-N40 [ 3276 ]	580	590	600	610	620
OspA-ZS7 [ 3264 ]	580	590	600	610	620

FIGURE 42 (11 of 16)

OspA-25019 [ 2802 ]	5 580	590	600	610	620 c. caa>
•	580	590	600	610	<b>65.</b>
OSDA-K48	580	590	son	610	620 . tcc. cag> 620 cc. cag>
OSDA-HE 11	.580	590 . 6	ino.	610	620 . tcg>
OSDA-DK29	580	590 6	ດດ	610	620 cc. cgg>
					620 620 c. c. cag>
OspA-BO [ 2558 ]	580	590	600	. 610	
OSPA-IP3 [ 2558 ]	580	590	600	610	
OspA-PKO [ 2558 ]	580	590	600	610	
Ospa-acai [ 2556 ]					620 .cc. cag>
ospa-P-GAU [ 2544 ]	- 580	590 a a	600		
Ospa-B31	GCI ACI AAA	640 AAA ACT GCA GC	ארישים הדולות בביצות דו	000 100	
OspA-B31 - [ 3288 ]	- 630	640	650	CCG TGA AGT	TGA AAT TGT
Ospa-Ka [ 3288 ]	630	640	650	660	>
Ospa-N40 [ 3276 ]	630	640	65n ·		-
Ospa-ZS7 [ 3264 ]	630	640	650	660	670
OspA-25015 2802 ]	630	640	650	660	··· ··· ···> 670
)spA-TRO 2648 ]	630	640 g. aaa	650	660	670
	•		· · · · · · · · · · · · · · · · · · ·	aat	

FIGURE 42 (12 of 16)

OspA-K48 [ 2584 ]	630	640 g.	650 aaa g	660 aaa	670 c >
OspA-HE 11 [ 2580 ]		640 t.c .g.	650 a.a g	660 t	670 t>
OSDA-DK29 [ 2566 ]	630	640 g.	650 aaa g	660 aag	670
OspA-Ip90 [ 2562 ]	630	640 g.	650 a.a g	660 . aag	670
OspA-BO [ 2558 ]	630	640	650 ·	660	670
OSPA-IP3 [ 2558 ]	630	640		660	
OspA-PKO [ 2558 ]	630	640	650	560	620
Ospa-ACAI [ 2556 ]	630	640	650 a g	660	670
ospA-P-GAU [ 2544 ]	630-	640	650	560	
	680	690		710	720
OspA-B31	ATT ACT GTA TAA TGA CAT	AAC AGT AAA A	AAA ACT AAA GAC MTT TGA TTT CTC	. Cuts cuts man	ACA AAA GAA TGT TTT CTT
OspA-B31 [ 3288 ]	680	690	700	710	720
Ospa-ka [ 3288 ]	680	690	700		720
Ospa-N40 [ 3276 ]	680	690	700	710	720 ···· >
OspA-ZS7 [ 3264 ]	680	690	700	710	720
Ospa-25015 [ 2802 ]	680	690 ac	700 c.	710	720 c>
OspA-TRO [ 2648 ]	680	690	700 a	710	. 700
OspA-K48 [ 2584 ]	680 gg.	690 .tc c	700 c a	710 ac	720
OspA-HE 11 [ 2580 ]	680 g. aa	690	700 c.a	710 .	720
Ospa-DK29	680	690	700	710	720

FIGURE 42 (13 of 16)

[ 2566 ] .	ggtc cc aac	>
OspA-Ip90 [ 2562 ]	680 690 700 710 ggtc cgc a ac	720 >
OspA-B0 [ 2558 ]	680 690 700 710 gtcc. c.a	
OSPA-IP3 [ 2558 ]	680 690 700 710 gtc. c.a	720 t c>
OspA-PKO [ 2558 ]	680 690 700 710gtcc. c.a	720
Ospa-ACAI [ 2556 ]	680 690 700 710	720 t c>
ospA-P-GAU [ 2544 ]	680 690 700 710 gtc	720 t c>
		50
OspA-B31	AAC ACA ATT ACA GTA CAA CAA TAC GAC TCA AAT GGC ACC TTG TGT TAA TGT CAT GTT GTT ATG CTG AGT TTA CCG TGG	AAA TTA GAG TTT AAT CTC
OspA-B31 [ 3288 ]	730 740 750 76	
Ospa-Ka [ 3288 ]	730 740 750 76	
OspA-N40 [ 3276 ]	730 740 750 76	io >
OspA-ZS7 [ 3264 ]	730 740 750 76	0 >
OspA-25015 [ 2802 ]	730 740 750 76 g tca gcaa	cga>
OspA-TRO [ 2648 ]	730 740 750 76 g a gca	0
Ospa-K48 [ 2584 ]	730 740 750 760 ga a gca	770 t ca>
OspA-HE 11 [ 2580 ]	730 740 750 76 g a.c gca	
OspA-DK29 [ 2566 ]	730 740 750 760 gaaggca	770 t ca>
OspA-Ip90 [ 2562 ]	730 740 750 760 gaagca	770 t ca>
OspA-BO [ 2558 ]	730 740 750 76 gatac.gcat	

FIGURE 42 (14 of 16)

OSPA-IP3 [ 2558 ·]	g	730 a't	• • • • •	740 · a	75	0 c gca	t	76	t	a>
Ospa-PKO [ 2558 ]	g	730 at		740 a	75	0 c gca			t	دة
Ospa-ACAI [ 2556 ]	g	730 at			7:			76		a>
ospa-P-GAU [ 2544_]	t	730 at	a	740	75		t			ده
•	770	780		790	*	800		•	810	• .
OspA-B31	GGG TCA CCC AGT	GCA GTT CGT CAA	GAA ATT	ACA AAA	CTT G	T GAA	ATT	AAA	AAC GCT	ATT AAA
OspA-B31 [ 3288 ]	770	780			•••	800	• • •		810	>
Ospa-Ka [ 3288 ]	770		•••	790	•••				810	>
Ospa-N40 [ 3276 ]	770	780		790		800		• • •	810	>
OspA-ZS7 [ 3264 ]	770	780		790 	•••••	800			810	>
OspA-25015 [ 2802 ]	770 c a	780 c		790 .ac.	•••	800	c		810	>
OspA-TRO [ 2648 ]	c aac			.ac.		• • • •	с	• • •		
OspA-K48 [ 2584 ]	c aa.						c	810	• • • • • • •	>
OspA-HE 11 [ 2580 ]	770 c aa.	780 c		790 c.	a	800 a		•••		>
OspA-DK29 [ 2566 ]		780 c		90 c.			с.,	810	•••	•••
OspA-Ip90 [ 2562 ]	c aa.	780 c		90 cg			c	810	g.t	>
OspA-B0 [ 2558 ]	•	780 C		790 .ac.			c		810	>
OSPA-IP3 [ 2558 ]	770 c a	780 		790 .ac.		800	с	•••	810	>
OspA-PKO [ 2558 ]	770 c a.	780 c		790 .ac.		800	c	<i>:</i>	810	>

FIGURE 42 (15 of 16)

Ospa-ACAI [ 2556 ]		a	780 c		•••	. 7	90 .c.	•••	800	c	•••	810	• • •	g>
ospa-P-GAU [ 2544 ]		a,	780 c		•••		90 .c.	•••	800	c	• • •	810	•••	>
÷ •														
	82	D •				٠								-
OspA-B31	AAA TTT I													•
Ospa-B31 [ 3288 ]	820													
Ospa-Ka [ 3288 ]	820												•	
Ospa-N40 [ 3276 ]	820			-										
Ospa-ZS7 [ 3264 ]	820							••						
OspA-25015 [ 2802 ]	.g.>		•				٠		\$ ⁷ *					
OspA-TRO [ 2648 ]	820													
Ospa-K48 8: [ 2584 ]	20	>												
OspA-HE 11 [ 2580 ]	820	.>												
OspA-DK29 82 [ 2566 ]	20	.>			-									
OspA-Ip90 82 [ 2562 ]	0 •••••	>					*	,				ونو م	***	
OspA-BO [ 2558 ]	820	>												
OSPA-IP3 [ 2558 ]	820	> ₁												
OspA-PKO [ 2558 ]	820	>							•					
OspA-ACAI [ 2556 ]	820	.>	,											
ospa-P-Gau [ 2544 ]	820	.>												•

FIGURE 42 (16 of 16)

. •	10		20		30		40
ATG AAA A TAC TTT T	TAT AA	TTA 7	TTG OGA	ATA GGT	CTA GAT	ATA TTA	GCC TTA ATA CGG AAT TAT
50	•	60	•	70		80	90
GCA TGT A	AG CAA IC GIT	AAT C	ETT AGC CAA TCG	AGC CTT	GAT CTA	GAA AAA CTT TTT	AAT AGC GTT TTA TCG CAA
•	100	•	110	*	120	*	130
TCA GTA GI AGT CAT C	ATT TA TAA AT	CCT C	ADO TOS	ATG ACA	CAA	CTT GTA GAA CAT	AGT AAA GAA TCA TIT CIT
140		150 *	*	160	•	170	180
AAA GAC AI TTT CTG T	NA GAC	CCA T	AA TAC	AGT CTA TCA GAT	SAS CTC	GCA ACA	GTA GAC AAG CAT CTG TTC
•	190		200		210		220
CTT GAG CT GAA CTC G	AAA TY TTT AA	GGA A	CT TCT	GAT AAA	AAC	AAC GGT TTG CCA	TCT GGA ACA AGA CCT TGT
230	*	240	₹.	250·	•	260	270
CTT GAA GO GAA CTT CO	et gaa La cit	A AAA T TTT	ACT GAC	AAA AGI TTT TCA	AAA	GTA AAA CAT TIT	TTA ACA ATT AAT TGT TAA
•	280		290	•	300		310
GCT GAT GU	AC CTA	AGT C	CAA ACT	AAA TTT	GAA	ATT TTC TAA AAG	AAA GAA GAT TTT CTT CTA
320		330		340		350	360
OCC AAA AC COG TTT TO	ATTA TEA	GTA T CAT A	CA AAA GT TTT	AAA GTA TTT CAT	ACC TGG	CTT AAA GAA TTT	GAC AAG TCA CTG TTC AGT
*	370 *		380		390	•	400
TCA ACA GA AGT TGT CT	A GAA	T AAA A TTT	TC AAC AG TTG	GAA AAG CTT TTC	GGT CCA	GAA ACA CTT TGT	TCT GAA AAA AGA CTT TTT
410	ŕ	420	•	430	•	440	450
ACA ATA GT TGT TAT CA	TA AGA	GCA A CGT T	AT GGA TA CCT	ACC AGA	CTT GAA	GAA TAC	ACA GAC ATA TOT CTG TAT
<b>*</b>	460	*	470	•	480		490
AAA AGC GI TTT TCG CT	NT OGA TA CCT	TCC G AGG C	GA AAA CT TTT	GCT AAA CGA TTT	GAA ÇTT	GTT TTA CAA AAT	AAA GAC TTT TTT CTG AAA
500	*	510	*	520	*	530	540
ACT CTT GI TGA GAA CT	AA GCA	ACT C	TA GCT	GCT GAC	CCG	AAA ACA	ACA TTG AAA TGT AAC TIT
•	550	•	560	•	570		580
GTT ACA G	AA GGC	ACT G	TT GTT	TTA AGC	AAG	AAC ATT	TTA AAA TCC

K48/Tro OBDA
Wednesday, April 27, 1994 11:37 AM
CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TTG TAA AAT TTT AGG

590 600 610 620 630

GGA GAA ATA ACA GTT GCA CTT GAT GAC TCT GAC ACT ACT CAG GCT CCT CTT TAT TGT CAA CGT GAA CTA CTG AGA CTG TGA TGA GTC CGA

640 650 660 670

ACT AAA AAA ACT GGA AAA TGG GAT TCA AAT ACT TCC ACT TTA ACA TGA TTT TTT TGA CCT TTT ACC CTA AGT TTA TGA AGG TGA AAT TGT

680 690 700 710 720

ATT AGT GTG AAT AGC AAA AAA ACT AAA AAC ATT GTA TTT ACA AAA TAA TCA CAC TTA TCG TTT TTT TGA TTT TTG TAA CAT AAA TGT TTT

730 740 750 760

GAA GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTT CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA

770 780 790 800 810

CTA GAA GGC AAC GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA GAT CTT CCG TTG CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT

820

AAC GCT TTA AAA TAG TTG CGA AAT TTT ATC

Figure 43 (2 of 2)

	10	20		30	•	40
ATG AAA AA TAC TTT TT	AIT TAT A TAA ATA T	TTG GGA AAC CCT	ATA GGT TAT CCA	CTA ATA GAT TAT	TTA GCC	ATA ATA TAT TAA
50	60	•	70	•	80	90
GCA TGC AA CGT ACG TT	G CAA AAT C GTT TTA	CAA TOG	AGC CTT TCG GAA	GAT GAA CTA CTT	AAA AAA YIT TIT	AGC GCT TCG CGA
•	100	110	*	*	*	130
TCA GTA GA AGT CAT CT	T TTG CCT A AAC GG	CCA CIC	ATG AAA TAC TTT	CAA GAA	CAT TO	T AAA GAA A TTT CTT
140	150	• ' • ,	160	*	170	180
AAA GAC AA TTT CTG TT	A GAC GG	T AAG TAC A TTC ATG	AGT CTA	AAG OCA	TGT CA	A GAC AAG T CTG TTC
•	190	200	*	210	*	220
ATT GAG CT	TA AAA GG AT TTT CC	A ACT TCI ADA ADT T	GAT AAA	GAC AAT CTG TTA	CCA AG	T GGA GTG A CCT CAC
230	-	* *	250	•	260	270
CTT GAA GO GAA CTT CO	ST ACA AA CA TGT TI	A GAT GAC T CTA CTC	AAA AGT	TAAA GCA	TT AAA 17 AA TIT A	'A ACA ATT AT TGT TAA
	280	290	•	300	*	310
GCT GAC G CGA CTG C	AT CTA AC TA GAT TO	T AAA AC A TIT TG	C ACA TIN G TGT AA	C GAA CIT C CIT GA	LA ATT T TAA A	AA GAA GAT TT CTT CTA
320	33	0	340	*	350	360
GGC AAA A CCG TTT T	CA TTA GT GT AAT C	ng toa ag No agt to	a aaa gt t tit ca	a agt tc t tca ag	T AGA G A TCT C	AC AAA ACA NG TIT TGT
•	370	380		390	•	400
TCA ACA ( AGT TGT (	BAT GAA A' TA CTT T	ng the aa ac aag th	T GAA AA A CTT TT	a GGT GA T CCA CT	A TTG T T AAC A	CT GCA AAA GA CGT TTT
410	4: *	20	430	*	440	450
ACC ATG I	aca aga g NGT TCT C	AA AAT GO TT TTA CO	ia acc ai It tgg tt	A CTT GA TT GAA CT	A TAT A I ATA T	CA GAA ATG GT CTT TAC
•	450	470	)	480	•	490
AAA AGC	GAT GGA A CTA CCT I	CC GGA AV GG CCT T	AA GCT AI FT CGA T	AA GAA GI	A ATT TI TAA AA	AA AAG TTT
500 *	•	310	520	•	530	540 * *
act ctt tga gaa	GAA GGA A	AA GTA G	CT AAT G GA TTA C	AT AAA G TA TTT C	TA ACA : AT TGT :	ITG GAA GTA AAC CTT CAT
1	550 *	56	0	570	•	580
aaa gaa	GGA ACC	ett act t	TA ACT A	ag gaa a	TT GCA	aaa tot gga

. 2.

129/133

P-GAU/BO-OSPA Wednesday, April 27, 1996 11:22 AM

TIT CIT CCT TGG CAA TGA AAT TCA TTC CIT TAA CGT TIT AGA CCT 600 620 GAA GTA ACA GTT GCT CTT AAT GAC ACT AAC ACT ACT CAG GCT ACT CTT CAT TGT CAA CGA GAA TTA CTG TGA TTG TGA TGA GTC CGA TGA 660 650 AAA AAA ACT GGC GCA TOG GAT TCA AAA ACT TCT ACT TTA ACA ATT TTT TTT TGA CCG CGT ACC CTA AGT TTT TGA AGA TGA AAT TGT TAA 710 700 690 720 AGT GTT AAC AGC AAA AAA ACT ACA CAA CTT GTG TTT ACT AAA CAA TCA CAA TTG TCG TTT TTT TGA TGT GTT GAA CAC AAA TGA TTT GTT 740 750 730 GAC ACA ATA ACT GTA CAA AAA TAC GAC TCC GCA GCT ACC AAT TTA CTG TGT TAT TGA CAT GTT TTT ATG CTG AGG CGT CCA TGG TTA AAT 790 770 780 GAA GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC CTT CCG TGT CGT CAG CTT TAA TIT TGT GAA CTA CTT GAA TIT TTG

820

GCT TTA AAA TAG CGA AAT TTT ATC

Figure 44 (2 of 2)

	•	•		10		<b>.</b>	20			30	)	4		40	
AT AT	G AA	A	AAI	AT A	TT T	A TIV	3 GG: C CC:	A ATZ	CCI	CIA CAR	ATA TAT	TTZ	4 600	* TTI	ATA A TAT
	50 ±			*	6	0 .			70	4		80			90
ce. eci	A TG	T	AAC	CAI GT	AA?	I GI	AGC	AGC TCC	· ~	GAC	GAG CTC	AA. TTT	AAC	AGC	GTT CAA
	*			00	•	•	110		•	120				30	
TC2 AG1	CA	A	GAI CTA	AAC	CC1	/ CC3	GAA CIT	ATC	AAA TTT	GTT CAA	CTT GAA	GTA CAT	AGC	AAA	CAA CTT
	140				150	)	4		.60	_		170			180
AAA TI'I	AA A	C	aaa TTT	CTC	: GGC	AAC	TAC	GAT CTA	CTA GAT	ATT TAA	GCA CGT	ACA TGT	GTA CAT	GAC CTG	AAG TTC
	*			90	•		200			210			_	20	,-
CIT GAA	GA(	S	CTT GAA	AAA	CCI	ACT	TCT AGA	GAT CTA	AAA TTT	AAC TTG	AAT TTA	GGA CCT	TCT	GGA CCT	GTA CAT
	230			*	240		•		50			260			270
CTT GAA	GA!	r	CCC	GTA CAT	AAA	GCT CGA	GAC	AAA	7 Cm	AAA	GTA CAT	AAA TTT	TTA AAT	ACA TGT	± TTT KAT
	*		_	80	*		290			300				LO	
TCT AGA	GAC	3 (	gat Cta	CTA GAT	GGT CCA	CAA GTT	200	ACA TGT	CTT GAA	GAA CTT	GTT CAA	TTC	AAA	GAA	GAT
	320				330		_		40			50			360
CCC	AAA		aca Tgt	CTA GAT	GTA	TCA AGT	AAA TTT	AAA TTT	GTA: CAT	ACT TGA	TCC AGG	AAA TTT	GAC	AAG	*
			_	70			380			390			40		WG1
TCA AGT	ACA TGT	. (	GAA CTT	GAA CTT	* AAA TTT	TTC AAG	AAT TTA	GAA CTT	* AAA TTT	GGT CCA	GAA CTT	# GTA CAT		*	AAA www
	410				420		_	43				40			450
ATA TAT	ATA TAT		ACA PGT	aga TCT	GCA	AAT TTA	GGA CCT	acc Tgg	AAA TTT	CTT GAA	GAA CTT	TAT ATA	ACA TGT	* GAA CTT	ATG TAC
	*		46		*		70		_	480			49		
AAA TTT	AGC	(	TAE	GGA CCT	ACC TGG	GGA CCT	444	GCT CGA	AAA TTT	GAA CTT	GTT CAA	TTA AAT	AAA TTT	* AAG TTC	t TTT AAA
	500 *			*	510		_	52				30		-	540
ACT TGA	CTT GAA	0	AA	GGA CCT	AAA	GTA CAT	GCT CGA	AAT ATT	GAT CTA	AAA TTT	GTA . CAT	* ACA TOT	TTG AAC	¢ GAA CTT	# GTA CAT
	*		55		*		60		•	570			58	0	
AAA	GAA	C	GA.	ACC	GTT	ACT	TTA	AGT	AAG	GAA	ATT	TCA	AAA	* TCT	ecc

B31-PBK nednesday, April 27, 1994 11:19 AK

820

GCT TTA AAA TAA CGA AAT TTT ATT

TIT CIT CCT TGG CAA TGA AAT TCA TTC CIT TAA AGT TIT AGA CCC 630 620 GAA GIT TOA GIT GAA CIT AAT GAO ACT GAO AGT AGT GOT GOT ACT CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA TGA 660 650 AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA ATT TIT TIT TGA CGT CGA ACC TTA AGT TIT TGA AGG TGA AAT TGT TAA 700 710 690 680 AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT 750 730 740 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT 800 780 770 GAA GOC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC CTT CCG TIT CGT CAG CIT TAA TGT TGT GAA TIT CTT GAA TIT TTG

Figure 45 (2 of 2)

			,	
10	2	20	30	40
ATG AAA AAA TAC TIT TIT AAT	TAT TTA TTG G ATA AAT AAC C	GA ATA GGT CT TAT CCA	CTA ATA TTA GAT TAT AAT	פרר דדא אדא
50	60	70	80	90
GCA TGC AAG C CGT ACG TTC C	CAA AAT GIT A GIT TTA CAA T	AGC AGC CTT	GAT GAA AAA	AAC AGC COM
100	. 11	.0	120	130
TCA GTA GAT T AGT CAT CTA A	ito cct got g Vac gga cca c	AAA DTA DAA TTT DAT DT	GTT CTT GTA CAA GAA CAT	AGT AAA GAA TCA TTT CTT
140	150	160	170	180
AAA GAC AAA C	FAC GGT AAG T	AC AGT CTA	AAG GCA ACA	GTA GAC AAG CAT CTG TTC
190	20	00	210	220
ATT GAG CTA A	AAA GGA ACT T PTT CCT TGA A	CT GAT AAA GA CTA TTT	GAC AAT GGT CTG TTA CCA	TCT GGA GTG AGA CCT CAC
230	240	250	260	270
CTT GAA GGT A GAA CTT CCA T	ACA AAA GAT G NGT TTT CTA C	AC AAA AGT TG TTT TCA	AAA GCA AAA	TTA ACA ATT AAT TGT TAA
280	29	70	300	310
GCT GAC GAT C	CTA AGT AAA A SAT TCA TIT T	ACC ACA TTC ACG TGT AAG	GAA CTT TTA	AAA GAA GAT TTT CTT CTA
320	330	340	350	360
GGC AAA ACA T CCG TTT TGT A	TTA GTG TCA A AAT CAC AGT T	AGA AAA GTA	AGT TCT AGA TCA AGA TCT	GAC AAA ACA CTG TTT TGT
370	38	30	390	400
TCA ACA GAT O AGT TGT CTA O	SAA ATG TTC A CTT TAC AAG T	AT GAA AAA TA CTT TTT	GGT GAA TTG CCA CTT AAC	TCT GCA AAA AGA CGT TTT
410	420	430	440	450
ACC ATG ACA A TGG TAC TGT T	AGA GAA AAT G	EGA ACC AAA ECT TGG TTT	CTT GAA TAT	ACA GAA ATG TGT CTT TAC
460	47	70	480	490
AAA AGC GAT ( TTT TCG CTA (	ega acc ega a ect teg cct t	AAA GCT AAA TT CGA TTT	GAA GTT TTA CTT CAA AAT	AAA AAG TIT TIT TIC AAA
500 *	510	520	530	540
ACT CTT GAA ( TGA GAA CTT (	GGA AAA GTA G CCT TTT CAT C	CT AAT GAT CGA TTA CTA	AAA GTA ACA TTT CAT TGT	TTG GAA GTA AAC CTT CAT
550	0 56 * *	5C * *	570	580
aaa gaa gga j	ACC GTT ACT I	DAA TOA ATT	GAA ATT TCA	

TIT CIT CCT TGG CAA TGA AAT TCA TTC CTT TAA AGT TTT AGA CCC GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT GCT ACT CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA TGA AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA ATT TIT TIT TGA CGT CGA ACC TTA AGT TIT TGA AGG TGA AAT TGT TAA AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT 740 750 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT 790 770 780 800 810 GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG OCT TTA AAA TAA CGA AAT TIT ATT

Figure 46 (2 of 2)

#### INTERNATIONAL SEARCH REPORT

intel al Application No PCT/US 94/12352

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 C12N15/31 C12N1 C12N15/62 C07K14/20 A61K39/02 G01N33/50 C07K16/12 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 6 C07K C12N A61K GO1N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category * Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X MOLECULAR MICROBIOLOGY, 1,6,7,9, 22,27, vol.6, no.20, 1992 pages 3031 - 3040 28,30,45 ROSA P. A. ET AL. 'Recombination between genes encoding major outer surface proteins A and B of Borrelia burgdorferi! see the whole document X Further documents are listed in the continuation of box C. Χ Patent family members are listed in annex. Special categories of cited documents: later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the document defining the general state of the art which is not considered to be of particular relevance earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docudocument referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report n 3. 03. 95 24 February 1995 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Espen, J Fax: (+31-70) 340-3016

Form PCT/ISA/210 (second sheet) (July 1992)

		PCT/US 94/12352
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
ategory	, Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
O, X	GINSBERG H. S. ET AL. (EDS.) 'Vaccines 93.  Modern approaches to new vaccines including prevention of AIDS. Tenth annual meeting, Cold Spring Harbor, New York, USA, September 1992.' 1993, COLD SPRING HARBOR LABORATORY PRESS, NEW YORK cited in the application McGrath B. C. et al.: 'Biochemical and biophysical characterization of the major outer surface protein from north american and european isolates of Borrelia burgdorferi' see page 365 - page 370 see page 369, last paragraph	1-4,10, 14,17, 22-25, 31,35,38
X	JOURNAL OF BACTERIOLOGY, vol.175, no.9, May 1993 pages 2516 - 2522 KITTEN T. ET AL. 'Intragenic recombination and a chimeric outer membrane protein in the relapsing fever agent Borrelia hermsii' see the whole document	1,6-8, 22,27-29
<b>Y</b> .	WO,A,93 08306 (SYMBICOM AKTIEBOLAG) 29 April 1993 see claims 44-46	1-9, 22-30, 45-48
Y	WO,A,91 13630 (THE UNITED STATES OF AMERICA) 19 September 1991 see page 8; figures 11,13	1-9, 22-30, 45-48
P,X	WO,A,94 20536 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 15 September 1994 see page 4-6; claim 6	1,6,22, 27

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

#### INTERMITIONAL SEARCH REPORT

Information on patent family members

	<u> </u>
Inter	11 Application No
PCT/	US 94/12352

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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WO-A-9113630	19-09-91	AU-B- AU-A- CA-A- EP-A- JP-T-	645078 7496591 2077434 0524958 5501113	06-01-94 10-10-91 06-09-91 03-02-93 04-03-93
WO-A-9420536	15-09-94	AU-B-	6366894	26-09-94

Form PCT/ISA/218 (patent family annex) (July 1992)